

The unacceptable face of nationalism

Unless the fiercer manifestations of nationalism are subdued, European cooperation, in both politics and science, has no future.

THE proud image of France has taken a fearful battering in recent weeks, culminating in the public admission on Sunday by Prime Minister Laurent Fabius of the "bitter truth" that the French secret service, the DGSE, had sunk the *Rainbow Warrior*, flagship of the environmental organization Greenpeace, and moreover that the DGSE had acted "under orders". Whose orders, it is not yet clear, and it must be uncertain in such tangled affairs whether even the parliamentary inquiry requested by M. Fabius will arrive at the final, unvarnished truth of the matter. As M. Fabius well knows, socialist members will wish to protect their government; and the right wing will protect the DGSE and the extreme nationalistic sentiments it represents, along with the nuclear deterrent and the glory of France. In the secret service of any government, be it French, British, American or Soviet, truth and fiction are interchangeable at many levels.

But above this noise, there is one clear signal: rampant nationalism has gone too far. Sentiments have been voiced and acted upon in France that raise "the nation" into the same kind of radiant divinity, bearing no relation to reality, that has motivated far worse crimes in human history than France's single, unintended murder in Auckland — however abhorrent that crime might be.

France, of course has long had a reputation for being strongly nationalistic — and not just among the British who seem to find the French strangely attached to their own language. Let us be clear immediately, post-war history shows that France is not alone in its excessive pride — surely Britain and France together are the nationalists of Europe, both resting culturally on the laurels of empire — but it is France, for the moment, that has brought itself into the public eye. And France has been nationalistic not only to its nuclear weapons testing in the South Pacific, and its consequent attack on the *Rainbow Warrior*, but also in another area of its policy, that of European cooperation in research and technology.

Eureka

Thus Eureka, the French initiative in European cooperation in the development of new high technology products, while avowedly European, has been compromised by French attempts to dominate the programme. France, it seems, wishes to see a new Europe, provided it is led by France. How else is it possible to interpret the strong French effort at the first ministerial meeting on Eureka this spring to set up a Eureka secretariat in Paris, despite an avowed French intention that Eureka projects should have *ad hoc* management structures? Britain rejected the proposal. How else can one interpret the French attitude to the European advanced fighter concept (the EFA), of which again France wished to have the lion's share, and which France finally left to the rest of Europe to develop while its own manufacturers went their own way?

How else, furthermore, can one interpret the mysterious French insistence that the European Commission shall not be involved in Eureka? Here the arguments are many, but it was clear from the beginning that Eureka had hijacked the whole spirit of the commission's Esprit programme in information technology, which had been brilliantly set up by the Belgian ex-commissioner Etienne Davignon. Yet it seemed many

months before French research minister Hubert Curien reluctantly admitted his debt. The European Commission feels "by-passed" by Eureka. The argument for this position is that the Commission is too slow and bureaucratic. But if this is so it is often because the Council of Ministers — the representatives of the nation-states of Europe — tamper with Commission initiatives until they become too watered down, too late or too little (thus it was with biotechnology). What, then, will be different about Eureka? Will not the nationalistic sentiments that the European Community was precisely founded to calm, and which are so evident in the Greenpeace affair, get greater rein?

Eureka proponents talk of "flexibility" and "variable geometry" — which means different nations can participate in different projects, and that nations outside the EEC can join in. But the former was already the case under Esprit, and the latter under many long-standing Commission programmes in the COST (cooperation in science and technology) umbrella. Why, then, is Eureka by-passing the European Commission? Is it realism? Or is it really a nationalism which will threaten to fragment true cooperation?

Remedies

We shall see how things turn out at the next ministerial meeting on Eureka in Hannover in November. And may they turn out well, for finally there is only one cure for excessive attention to the national interest, and that is the creation of an international interest. Thus only when more and more jobs, and with them political power and influence, begin to depend on true European collaboration, will a real Europe emerge and the old jingoisms subside. It is a thought that applies just as well to the North-South divide — and in particular to France and the South Pacific. There, President Mitterrand has warned that he will defend the French national interest in the weapons tests on Muroroa atoll "by force", against a new Greenpeace flotilla now converging on the area. It might be better for French interests in the rapidly growing economy of the Pacific, and for world harmony, if he took a more pacific, and economic, line.

But glory is France's, and perhaps even America's, constitutional dilemma. As George Orwell, the British socialist writer, once pointed out, the advantage of a constitutional monarchy is that it succeeds in separating the glory of kingship from the power of government. In France, de Gaulle's presidential constitution combines both. It was once said — by a Frenchman — that France is a kingdom, but Britain a republic. And now that the survival of President Mitterrand's presidency into its final two years is surely threatened by the Greenpeace affair, perhaps there is a chance for some constitutional amendment — not, of course, to restore a monarchy, but at least to reduce the glory of the presidency by reducing the term of office from seven years to the present five years the government enjoys.

In the United States, it was the impeachment of President Nixon over the Watergate affair that moderated the glory of the presidency, and marked out the limits of its power; in France it may not be any Greenpeace investigation *per se* but a little constitutional amendment down the line that is what the doctor ordered. □



Strategic Defense Initiative

Star wars criticized by OTA report

Washington

THE US Congress's Office of Technology Assessment (OTA) has added its voice to those critical of President Reagan's Strategic Defense Initiative (SDI). In a major report published this week (*Ballistic Missile Defense Technologies*), OTA concludes that SDI offers an opportunity to increase substantially US national security only if the research programme achieves "great technical success" and if the Soviet Union cooperates in a negotiated reduction of strategic nuclear weapons. On the other hand, SDI carries the risk that a vigorous anti-ballistic missile research programme could lead to a race for both offensive and defensive arms, and a further risk that development

of a "star wars" type defence without Soviet cooperation could create severe strategic instabilities.

OTA says its report is intended to illuminate, rather than to adjudicate, the debate over star wars. The report critically examines the assumptions that lie behind many of the oft-quoted benefits — and dangers — of SDI, but necessarily stops short of providing firm answers to many of the questions raised.

But OTA notes that although President Reagan's original "star wars" speech of March 1983 referred to a means of rendering nuclear weapons "impotent and obsolete", the administration seems now to accept OTA's assessment that "assured survival of the US population appears impossible to achieve if the Soviets are determined to deny it to us". However, OTA grants that strategic defences might be plausible for limited purposes such as the defence of missile silos or to complicate of enemy attack plans.

Although many of OTA's conclusions are framed in cautious language, there is no doubt that it will be hailed by opponents of SDI as a vindication of their position. More recent pronouncements by President Reagan on SDI have emphasized its usefulness as a means of persuading the Soviet Union to negotiate seriously over reducing nuclear arms: OTA says, however, that it is "unable to find anyone who could propose a plausible agreement for offensive arms reductions and a coop-

erative transition that could be reached before both the Soviets and the United States learn more about the likely effectiveness and costs of advanced ballistic missile defences . . . such a transition could hardly be planned until engineering development was well advanced on the actual defensive systems to be deployed. Even then, verification would be difficult".

The essence of the problem, according to OTA, is whether a vigorous US research programme, with the prospect that both sides might eventually deploy a defensive system, would make the Soviet Union more willing to negotiate deep reductions in offensive weapons. If no agreement could be reached deployment could trigger a further build up of weapons. Commenting on the OTA study this week, chairman Les Aspin of the House of Representatives Armed Services Committee said that "even if both the United States and the Soviet Union have a strategic defence system, the world could end up less safe than now". Aspin pointed out that although SDI might allow a proportion of US strategic defences to survive a Soviet first strike, its usefulness would be open to question if the Soviet Union also had a defensive system.

OTA has also just published an assessment of anti-satellite weapons (*Antisatellite Weapons, Countermeasures, and Arms Control*). It concludes that while arms control might reduce the threat from Soviet anti-satellite weapons, decisions to deploy such weapons should wait until the administration decides whether to go ahead with an anti-missile system, since any plausible anti-missile system would also have excellent anti-satellite potential.

Tim Beardsley

Premature death?

Washington

THE US Department of Defense (DoD) admitted last week that the scientific satellite destroyed two weeks ago in a successful anti-satellite test was not, as previously described, "obsolete". The satellite was transmitting useful data on the solar corona up until the moment it was destroyed, according to Robert MacQueen of the High Altitude Observatory at the National Center for Atmospheric Research.

The Air Force satellite, which is known as P78-1, was carrying four instruments, according to DoD: a coronagraph, called "Solwind", which was still functional at the time of the test; an X-ray monitor, from which data returns were said to be "marginal" due to degraded power supplies; an ultraviolet spectrograph and photometer, which was partly inoperable at the time of the test; and a solar X-ray instrument that had been inoperable for several months. DoD says P78-1 was chosen as a target because it had operational telemetry that allowed an independent test of when the anti-satellite destroyed it. The satellite had already exceeded its designed lifetime and ground support for the satellite was due to have been discontinued in 1987.

MacQueen is not so dismissive of the value of P78-1. Data from the coronagraph, he says, were complementary to those obtained from the National Aeronautics and Space Administration's Solar Maximum satellite.

DoD revealed details of P78-1's functions only after written requests from the *Washington Post*. A spokesman denied there had been any inconsistency in the satellite's characterization, saying "obsolete" referred only to the suboptimal rate of data production.

Tim Beardsley

Aspects of the Mexican earthquake

TIME: 13:17:45.4 UTC; hypocentre: 18.1°N, 102.3°W; (M_s): 7.8. These are the hard facts from the US Geological Survey about the earthquake that devastated Mexico City on 19 September. The main earthquake was followed the next day by an aftershock with $M_s=7.3$, with a hypocentre at 18.0°N, 101.5°W. This is towards the upper end of severity of expected aftershocks, according to the British Geological Survey (BGS). A further minor aftershock occurred on 23 September at 0945 UTC with $M_s=4.0$, and there will be thousands of tremors below detection limits.

The hypocentres of both major shocks lie tens of kilometres landward of the trench where the Cocos plate (essentially a breakaway piece of the Pacific) is being subducted under the North American continental plate. They are both reported as "depth normal", that is, the epicentre is nominally at 33-km depth, though the concept of a centre is not very meaningful for such large earthquakes. Records at the

International Seismological Centre at Newbury, UK, show a lot of energy at long periods, which implies that the seismic moment was high. The moment is a more direct measure of the total energy involved in an earthquake than is the magnitude, as it takes into account not only the displacement, but also the rigidity and the fault area. For this earthquake, the fault is likely to be quite large and may have broken the surface, says BGS.

The disproportionate destruction of Mexico City happened because the city stands on a thick pile of unconsolidated Quaternary lake sediments and volcanic ashes deposited in an intermontane basin. The region is effectively a continuation of the Basin and Range tectonic province of California, whereas the coastal area is composed of older, harder rock. The soft lake sediments have a lower acoustic impedance than the underlying rocks, the effect of which is to increase the amplitude of the displacements for the same amount of energy.

Peter Gambles

Dutch budget

Eureka needs to grow

Waalre, The Netherlands

INTERNATIONAL cooperation, including full support for Eureka, the European high-technology research programme initiated by France in April, forms a major plank of the Dutch government's science budget, presented to parliament last week by education and sciences minister Wim Deetman. Rumours of coolness towards Eureka were discounted by Deetman, who says that Eureka is an important initiative on the road to the "Technological Europe" envisaged by Prime Minister Ruud Lubbers when speaking at the European summit in April.

This enthusiasm for the European technological cause is likely to be continued when the Netherlands takes its turn at EEC chairmanship beginning in January 1986. The Dutch themselves now claim to be doing 1 per cent of the world's research, and Eureka, together with European Community programmes such as Esprit, BRITE and RACE, is seen as a logical step towards maintaining the country's research base.

The Dutch government feels, however, that Eureka should be broadened out to include countries outside the European Community, but that some link should also be made with the European Commission in Brussels. The Dutch science minister will be discussing Eureka with French minister M. Hubert Curien when they

meet in Germany next month. The Dutch view is that if it is to be worthwhile, Eureka should be flexible enough to include basic research and complex, ambitious projects that might otherwise go unsupported.

In the science budget, it is announced that the Dutch are to take part in research in Antarctica, probably in a joint venture with West Germany. The Netherlands is also likely to be a partner (through the European Science Foundation) in the Ocean Drilling Program. The year-long oceanographic expedition to Indonesia is described as a success, and the scientific results will be discussed at an international symposium to be held in Jakarta in 1987. Further bilateral projects, in cooperation with India and China, should start soon.

In the Netherlands itself, Deetman is to set in motion a study of Dutch science policy intended "to seek especially the weak points".

The total science budget is 8,200 million guilders, 4,000 million of which comes from government sources. The rest comes from industry, mainly the Dutch-based multinationals such as Philips and Shell. Expressed as a percentage of gross national product, science spending for 1985-86 is to be 2.13 per cent, compared with 2.10 per cent in 1984-85. The government's share of this is remaining constant, at 0.96 per cent for both years.

Casper Schuurin

A magnet for the Supercollider

Washington

THE central design group of the proposed Superconducting Supercollider (SSC) last week announced its choice of magnet design for the accelerator. It will be the high-field (6 tesla) cos θ type, which was chosen over the competing 3-tesla superferric design. A special magnet selection panel appointed to advise the design group concluded that "the hope of two years ago that the superferric magnet would provide a less costly SSC has not come true".

The superconducting magnets represent a major fraction of the total cost of SSC, currently estimated at about \$3,000 million. Superferric magnets, which have for the past 18 months been under intensive development at the Texas Accelerator Center, would at \$400 million be substantially cheaper than high-field magnets, estimated to cost \$1,000 million. But if SSC used superferric magnets the tunnel would need to be 100 miles in circumference, compared with just 60 miles with high-field cos θ magnets. The extra tunnelling cost associated with the superferric design was a major factor against it; in addition, the panel concluded that substantially more development work remained to be done on superferric designs than on the cos θ

magnets, which are used in all accelerators in operation or under construction.

Peter McIntyre of Texas Accelerator Center, who has devoted much of the past two years to working on the losing design, is unrepentant. He remains convinced that superferric magnets would still lead to a cheaper SSC if a site was chosen where tunnelling costs were low; six such sites have been identified in Texas and there are others in many states, says McIntyre. He will continue to perfect the superferric design for other applications while simultaneously working on high-field magnet development for SSC. The successful high-field design is the result of work at Fermilab, Brookhaven National Laboratory and Lawrence Berkeley National Laboratory.

The Department of Energy, which would foot the bill for SSC if it is ever built, has still made no formal commitment to the plan. A final decision will be made after a construction plan has been drawn up next spring, when more reliable cost estimates should be available. The latest guess is that the department will back the proposal if the likely cost is in the region of \$3,000 million, but that it will be obliged to drop the idea if SSC cannot be built for less than \$4,000-\$6,000 million. Tim Beardsley

Polish agriculture

Fight for control of peasant aid

POLAND'S controversial "Agricultural Foundation", established under church patronage to assist the recovery of private agriculture (see *Nature* 313, p. 5; 1985) moved a few steps closer to reality last week, when the Polish government waived its objection to church control of the fund. To save face, however, the government has said "no Polish citizen" may contribute to the fund. This is clearly a direct affront to Lech Walesa, who had pledged his winnings from the 1983 Nobel Peace Prize to the fund.

The church-sponsored team, headed by Dr Andrzej Stelmachowski of Warsaw University's law department, has sponsored a major research programme into Poland's agricultural needs and capabilities: Funds have been collected mainly in the United States and West Germany, and, says the church side, sufficient reserves were available in April to launch a pilot project during 1985. The government side, however, has consistently intimated that in its opinion insufficient money was yet available even to inaugurate a pilot scheme. It pressed, moreover, for the money to be placed under the control of the Ministry of Agriculture.

By mid-August, Cardinal Josef Glemp had clearly reached breaking point. In an interview with the Austrian daily newspaper *Kurier*, he stated that the scheme had "failed" because the government could not permit an independent group to become strong. He followed this up, two weeks ago, by telling the church negotiators that if the government did not relax its attitude, the church would have to cancel the whole scheme and would let the foreign donors know who was responsible. The Cardinal's remarks were relayed to the government, which then waived its demands for Ministry control over the funds and agreed to try and sort out the remaining major problem — whether agricultural equipment imported under the scheme would be liable to import duty.

Uniquely in the socialist bloc, some 75 per cent of all Polish land is in private hands, mostly in tiny peasant smallholdings. The private agricultural sector suffered considerably from pricing disincentives under the Gomulka and Giersek regimes and, although the security of tenure won during the Solidarity era gave the farmers the incentive to improve their holdings and adopt more modern agricultural practices, so far they have not had the resources. The Agricultural Foundation was designed to supply those resources, but so far the government has blocked their arrival. Last week's concessions may be genuine, or just related to the 13 October election to the Sejm (parliament).

Vera Rich

Technology poaching

US haunts for Soviet spies

Washington

THE Soviet Union has judged data obtained at Western scientific conferences to be "among the most significant" sources of information for its military development, according to a detailed assessment of West-East technology transfer published last week by the US government. The US report lists specific scientific societies and US universities that have been targeted by the Soviet Union for efforts to acquire research results with military applications.

Announcing publication of the report, Richard Perle, Assistant Secretary of Defense for International Security Policy and a known hardliner on technology transfer, said he hoped to "sensitize the scientific and technical community to the fact that there is a very large and well-organized Soviet apparatus that has targeted scientists and engineers and universities and the like for military purposes".

The report identifies two main components of the Soviet technology acquisition effort: one, managed by the Military Industrial Commission (VPK), seeks blueprints and one-off military and dual-use hardware samples for reverse engineering; the other, managed by the Ministry of Foreign Trade, seeks high-technology manufacturing and test equipment in bulk for direct use. An appendix to the report lists several hundred weapons that are claimed to have benefited directly. About 90 per cent of the documents acquired by VPK in the United States are not subject to security classification, however, and

Perle made plain his wish to see more militarily sensitive documents classified.

At least 35 scientific conferences worldwide were identified by VPK as sources of specific information during the late 1970s, according to the report. The more important include an international radar conference, a conference on integrated optics and a conference on aerospace and electronics systems held by the Institute of Electrical and Electronic Engineers. Universities selected for special attention from VPK's operatives include Carnegie-Mellon, Cincinnati, Harvard, Massachusetts Institute of Technology and California Institute of Technology. Liberal publication policies of the National Aeronautics and Space Administration are blamed for having led directly to identifiable Soviet gains in aircraft design.

According to some speculations, publication of the US report, prepared by the inter-agency Technology Transfer Intelligence Committee to update a 1982 assessment, was a result of the recent spate of spies defecting or being arrested. Perle seemed to hint as much when he said that circumstances that previously precluded publication of this amount of detail no longer applied. Some critics contend, however, that the timing of publication represents an attempt to catch up in the propaganda battle with the Soviet Union leading up to the Geneva summit in November.

Tim Beardsley

"Soviet Acquisition of Militarily Significant Western Technology: An Update" is available from the US Department of Defense.

Nuclear war

More gloomy forecasts

Washington

IMMEDIATE casualties resulting from a nuclear war, the subsequent short- and long-term physiological effects, and the long-term consequences to ecosystems have probably all been underestimated by the predictions in current use. But estimates are subject to gross uncertainties that can only be reduced by more research on the "biological effects" of a nuclear war. Much should be done by the US and Soviet governments to fund such research and to inform the public of the effects. These are the main conclusions at this week's meeting of the Institute of Medicine (IoM) at the National Academy of Sciences.

According to Dr Theodore Postel of Stanford University, a hypothetical attack of 100 one-megaton bombs on 100 US urban centres would cause 36-56 million immediate deaths, two to four times the number predicted by government studies based on blast effects alone. A one-megaton nuclear weapon can produce a fireball with a temperature of about 100 million °C at the centre, causing many simultaneous fires over hundreds of kilometres and hurricane-force winds. This fiery environment, together with the toxic smoke and combustion of gases, renders obsolete the "blast scaling" method of estimating the effects of a nuclear explosion used by government agencies.

One startling prediction of Postel's new "conflagration" model is that a major attack on US strategic nuclear targets would result in 16-35 million deaths and 9-41 million casualties even before the effects of fallout and damage to environmental and social systems are considered. These figures, from Dr Frank von Hippel and colleagues of Princeton University, are the outcome of the first calculations to have used computerized wind, target and population data bases apart from government studies, which are mainly classified.

The effects of toxic chemicals caused, for example, by burning of industrial plastics, is likely to have severe local consequences. Lofting of nitrogen oxides into the stratosphere would deplete the ozone layer, leading to increased ultraviolet radiation. Gases such as ammonia and methane could accumulate in the heavily polluted troposphere during periods of darkness.

Dr Frank Press, president of the National Academy of Science, summed up the general mood when he said that the "profundity of the consequences of nuclear war are such that symposia such as this . . . (provide a) most valuable public service". Dr Herbert Abrams of Stanford University called for more information to be provided by the US government for

Rebellion among the ranks

Washington

THE presidents of twelve major scientific and engineering societies last week informed Secretary of Defense Caspar Weinberger that their organizations would have nothing to do with the Pentagon's new policy of imposing restrictions on access at certain unclassified conferences. The societies pledged that they "will not be responsible for, nor will they sponsor, closed or restricted access technical sessions at meetings or conferences conducted under their auspices".

The strongly worded letter is a major setback for the Pentagon's efforts to stem the flow of technical information to Eastern-bloc countries. Earlier this year the Pentagon let it be known it intended to make routine use of export control laws to restrict foreigners' access to scientific and technical data which, although not subject to national security classification, might be of military significance. Such "export controlled sessions" are restricted to US nationals and to foreigners who are validated by their embassies; participants must undertake to keep the restricted in-

formation confidential. Export controls are applied only to research that is not considered "fundamental".

In their letter to Weinberger, the twelve society presidents say that the new controls have the effect of placing the controlled information *de facto* into a new category of classification. By limiting opportunities for peer review and open discussion of research, the presidents say, the restrictions are counterproductive and detrimental to national security.

Earlier this year the Department of Defense (DoD) caused a furore at a conference of the Society of Photo-Optical Instrumentation Engineers by imposing export controls at short notice, causing the conference to be entirely re-scheduled. Later, DoD declared itself happy with the idea of export-controlled sessions for "non-fundamental" data, which it saw as a more flexible alternative to security classification. Others, apparently, were not so happy; among the signatories of last week's letter is Lewis Larmore, president of the Society of Photo-Optical Instrumentation Engineers.

Tim Beardsley

public education and for a strengthening of screening tests to armed forces personnel because more than 5,000 personnel a year are removed from nuclear weapons handling duty because of drug abuse, alcoholism or psychological problems. The problem is likely also to be large in the Soviet Union, where alcoholism is a health problem of "epidemic proportions", he said.

The reluctance of the United States to consider the "biological" effects of nuclear war has been criticized by Dr Carl Sagan of Cornell University. Although the government in theory is providing \$50 million over 5 years to investigate the physical effects, no money is spent on biological research. One of the first studies on the ecological effects of a nuclear winter-like environment on plants is planned by Lawrence Livermore National Laboratory and the University of Wisconsin. But Dr Lynn Anspaugh of the former institute stressed the need for considerable resources to produce and continuously update an interactive model.

Maxine Clarke

UK atomic energy

Business not as usual

"WE'RE not just bench R&D; we have to be building things, getting things working". With this attitude the UK Atomic Energy Authority (UKAEA) moves into the final stages of negotiation over its reorganization into a trading fund, a change due to take effect at the start of its financial year in April 1986.

As chairman Arnold Allen announced at the presentation of the UKAEA annual report last week, trading fund status entails being run "as far as possible under the conditions of a normal commercial business" with payment for contracted work performance targets. Moreover, there will be an end to reliance on government grants to balance the books; this year UKAEA spent £399.7 million (up from £380 million) and was paid £174.4 million for its services (up from £169.6 million) with the difference provided by parliamentary vote. Remaining questions centre on "the precise financial regime" within which UKAEA will operate — the initial capital debt, borrowing ceiling and financing of basic research.

Contracts are an index of the authority's ability to get things working, according to Mr Allen. Those given to UKAEA comprise both nuclear contracts, including the supply of fuel and reactor insulation testing for the overseas market; and non-nuclear contracts, 13 per cent of UKAEA activity, which generated £30 million last year (up £2 million). Contracts worth £60 million were placed last year by the UKAEA Northern Division.

The authority's commitment to breeder reactors is evinced by its recent acquisition of a 49 per cent shareholding in Fast

Japanese exposition

Tsukuba Expo strikes camp

Tokyo

THE Tsukuba International Exposition, Japan's great high-technology extravaganza, has now closed its gates, having just squeezed past its self-declared target of 20 million visitors in its six-month run. Approximately one-sixth of the entire population of Japan — 20,334,727 people — made the effort to go and see the wonders that science has in store for them (see *Nature* 314, 213–220; 1985).

In setting the 20 million goal the Expo planners, with no experience of how popular the science theme might prove, took the view that the theme probably did not matter too much: it was simply assumed that attendance would be proportional to the size of the site. The 1970 Expo held near Osaka attracted 60 million visitors, so the Tsukuba Expo, on a site just one-third of its size, should attract 20 million.

Cynics might say that it is no wonder

that attendance turned out to be proportional to the size of the site — it was simply a matter of the physical limits of how many people can be packed into one space. But there may be a better explanation for why the 20 million goal was reached so neatly. Expo organizers knew they might otherwise come out in the red and in the past few weeks public enthusiasm has been whipped up with feverish campaigns. In a tremendous closing rally, one-third of a million people turned up on Sunday, breaking all previous records and pushing attendance to the 20 million mark.

For the Expo organizers, the attendance figures mean that they may end up with around ¥1,000 million (US \$4 million) in profits, which is not so bad. Things have not been so profitable, however, for the hundreds of small shops set up in the Expo grounds to sell souvenirs and food. Many have lost money heavily. Angry shopholders blame poor siting and bad organization, some are refusing to pay their rent and others are taking legal action.

The Expo's biggest hit was Fujitsu's three-dimensional computer-generated film which included an astonishing sequence of a DNA molecule being wound and rewound and packed into a chromosome. The theatre was completely full for almost every showing throughout the whole run. Biggest attendance figures of all were claimed by the Matsushita pavilion with more than five million visitors coming to see the portrait-drawing robot, which numbered Prime Minister Nakasone among its sitters.

Many foreign visitors were disappointed that there was so little substance to the Expo and so much spectacle; its aim sometimes seemed to be merely to accustom the Japanese people to a high-tech future whose coming had already been decided for them. But not only foreigners were critical: a group with considerable distrust of the intentions of the commercial electronics makers whose pavilions dominated the Expo launched their own alternative "AXPO 85" on a site nearby.

The Expo site is now to be cleared of its accumulated pyramids, cones, spheres and other fantastic structures in order to be turned into an industrial park. But some bits of the Expo will live on. The Chinese government is rumoured to be interested in buying some of the high-tech exhibits for a fair that will give the Chinese people a vision of what they are striving for. The Volvo articulated double shuttle buses are to go to Australia. And the Fuyo theatre's robots are likely to be bound for Disneyland in Florida. There, no doubt, they will feel much happier than they ever were at a science Expo. **Alun Anderson**

Reactor Technology (Fastec), a company set up to explore the commercial exploitation of the technology. The remaining shares are owned by National Nuclear Corporation. Fastec's prospects look particularly good because fast breeder reactors seem set to be less expensive than was assumed three years ago. The capital costs alone, said Dr Tom Marsham, a UKAEA board member, could be 20 per cent less than originally forecast. After start-up costs, the reactors are predicted to become "broadly competitive" with other sources of electricity.

UKAEA's research into fast reactor technology, centred at the Dounreay facility in Caithness, is now reaching fever pitch. Both the government and the authority hope that Dounreay will receive the European reactor club's nod of approval to reprocess spent plutonium from the demonstration reactors in France and West Germany. Britain's strongest case lies in its experience with reprocessing technology, one example of which is the £650,000 "pulsed column" rig at Dounreay for solvent extraction, said to be the largest sealed glovebox in the world.

Planning permission would have to come first and the Scottish Secretary, Mr George Younger, echoed the need for haste by limiting the inquiry, planned for early next year, to local issues. According to Dr David Locke of the Northern Division, an environmental assessment will be presented at the inquiry; but environmentalists see the move as preempting any concern besides that of the UKAEA to stay on top. **Elizabeth Collins**

Fast breeder reactors

And after Superphénix?

SUPERPHENIX, the European commercial-scale fast breeder reactor — and the world's largest — at Creys-Malville in southern France, is completing the loading of its plutonium core this week, after "going critical" for the first time on 7 September.

All has gone "very well" with low-power performance tests so far, according to the international agency NERSA that constructed the reactor, despite problems earlier this year with vibrations in the primary sodium cooling circuit (see *Nature* 315, p.269; 1985). The vibrations were "purely hydrodynamic", and were solved by a slight diversion of sodium flow within the core, an operation which set the Superphenix programme back by only three weeks, says NERSA.

Tests in the past two weeks have measured neutron spectra at a reactor thermal power of only 1 MW, and tested the operation of the control rod system, and all is now deemed well for a full loading of the core. Superphénix is due to be connected to the national grid at 20–30 per cent of its design 1,200-MW electrical power in January 1986, and to be brought up to full power by the spring. This will make Superphénix the world's most powerful fast reactor, followed by the Soviet Union's BN-600 (550 MW) which first produced power in 1980, and West Germany's SNR-300 (300 MW) which is due to go critical next year.

The next question in Europe will be what should follow Superphénix. Should it be Superphénix II, also in France? A French design for a 1,500-MW version which would be 40 per cent cheaper than Superphénix I is ready, and according to the French atomic energy agency (CEA) it would be possible to begin construction in 1987. According to the 1973 treaty between France, Italy, West Germany, the Netherlands and Belgium under which Superphénix I was constructed, West Germany should pay the lion's share of a second fast breeder, but now it seems that the French design is most favoured — and thus CEA would like to renegotiate the 1973 terms.

According to CEA, Superphénix II — or "project 1500" as it is now called — would shave costs by eliminating the containment vessel (because the previously "maximum credible accident", a catastrophic fast meltdown, is now considered "incredible"), and by large reductions in the length of the costly stainless steel cooling system.

As for the cost of Superphénix I itself, this was — according to NERSA — some FF 9,300 million (1977 prices), or around £1,000 million, excluding interest charges. This was partitioned 51 per cent to the French national utility, Electricité de France (EDF), 33 per cent to Italy, and 16

per cent to West Germany, the Netherlands, and Belgium. Each country will receive electricity from Superphénix in proportion to its stake, and according to EDF this will make Superphénix electricity about 2–2.2 times the price of that available from its existing pressurized water reactors. This will, however, only match the cost from the (admittedly expensive) EDF coal-fired plants, says EDF. The utility last week, however, refused to quote a capital cost for Superphénix, saying that "we are computing the cost" and that it was "too soon and deli-

cate" to be definitive.

Nevertheless, EDF is interested in future fast breeders "as a protection against a crisis in the uranium market". Uranium prices are now depressed, supply being much greater than the demand as the expansion in world nuclear power production predicted in the early 1970s and acted upon by uranium prospectors has simply not taken place. However, this could change in "10, 15, 20, even 5 years", EDF speculate: thus there is a strategic need to preserve the fast breeder option. The breeder would be economic competition for pressurized water reactors only if the uranium price was to increase 10-fold, however, EDF believes.

Robert Walgate

UK plant breeding research

In search of green thumbs

"ANYONE who takes the profits out of a plant breeding programme instead of putting them back in is not a plant breeder". By that definition the UK government has no green thumb: it has taken more profits out of the Plant Breeding Institute at Cambridge (PBI) than it has returned in financial support. Cuts in government support, which in 1986–87 alone amount to a shortfall of £180,000, have resulted in the internationally known institute for the first time in its history searching for private funds to support breeding programmes.

The search has been successful for triticale, a cross between wheat and rye which is used primarily for animal feed and grows well on marginal land. Given the grain surplus in the European Community, says Dr Peter Day, Director of PBI, these attributes also meant that the triticale programme was marked as one whose loss would "hurt least". Financial support for the programme will now be provided by Semundo, a plant breeding and seeds company with European breeding facilities and a UK branch primarily concerned with marketing. Semundo, says its general manager Christopher Green, sees "no limit to where the grain can be used"; its potential makes the risk of £600,000 over five years a good investment.

In return for its support, Semundo receives marketing rights to any new variety of triticale that is developed in the programme. The company can back out of the arrangement or move the programme away from PBI in five years, but neither possibility is likely. Semundo recognizes that plant breeding cannot be a short-term speculation, and it values the "technical excellence of the institute".

The long view necessary for plant breeding is exemplified in Dr Richard Gregory, who has led PBI's triticale programme since its beginning in 1970. The result so far is three varieties of triticale with plant breeder's rights (which means royalties are received on the seed), three

in second-year testing and two in first-year testing. Only this autumn will the first of the varieties be harvested for the seed trade.

While it was government funded, says Dr Gregory, the triticale programme tested its varieties only in Britain, thus choosing characteristics appropriate to the UK climate. Semundo involvement will encourage testing elsewhere in Europe and selection for hardiness and resistance to snow mould. A danger of too much private support, warns Gregory, is the loss of free exchange: competing companies would be unlikely to allow exchange of information or breeding material.

Since the announcement of cuts of £10 million each in the 1986–87 and 1987–88 Agricultural and Food Research Council (AFRC) budgets, the role of private companies in Britain's breeding programmes has been much debated.

One option now being considered is amalgamation of the 28 research institutes controlled by AFRC into a smaller number. Another option is to merge and privatize PBI with the National Seed Development Organization (NSDO), the marketing arm of government-funded plant breeding (see *Nature* 314, p. 2; 1985). After all, supporters point out, NSDO returned £2 million to the Treasury in its last financial year and 79 per cent of those profits come from PBI varieties. If NSDO alone were privatized (another proposed idea), it would be severed from its life source, "twitch for a while and then lie still".

Mr Derek Garner, Chief Executive of NSDO, says that merging NSDO and PBI "looks as though it could be done" but he sees no governmental moves in that direction. Without that direct a funneling of profits generated by PBI back into its breeding programme, the future of the institute, according to Dr Day, will rely on gaining support "from a wide base of private sector structures".

Elizabeth Collins

The AIDS panic

SIR—Public pressure for protective measures against acquired immune deficiency syndrome (AIDS) is only now starting to surface¹. Perhaps the greatest danger now is that the dramatic change in public attitudes towards the disease will have consequences more devastating than the syndrome itself. Growing demands for protection will force governments to adopt measures which, to be effective, may undermine the foundations of Western society, to the extent that they lead to segregation of the infected population, not only blood donors². The US army has already made a pioneering decision in that direction³.

A computerized listing of all seropositives used as a new basis for discrimination and eventual segregation of the potential viral carriers is not a fictitious danger. It is the logical outcome of the development of a fear for which the AIDS virus is less responsible than scientists and journalists. After accusing the sexual minority, rejected since biblical times by the prevalent religions, the authors of the sensational will now stress the number of victims⁴ and emphasize the hope for a vaccine (R. Gallo quoted in *Le Monde*), while the scientists, having exhausted the immunosuppressive properties of sperm, seminal fluid and homosexuality, now predict the danger of a lethal pandemic within the next 15–25 years⁵, forgetting that African AIDS, although appearing in 1970, has not fulfilled even part of the prophecy. The reasoning has been so simple as to appear flawless, as is always the danger with inductive science. A mere extrapolation from preliminary epidemiological data or other animal lentiviral diseases is sufficient to predict a pandemic in the 21st century, in the same simplistic way that for two years homosexuality was believed to be the cause of the syndrome, since AIDS was predominant in the homosexual population. The infectious agent hypothesis was then considered to be "too simplistic"⁶.

There is no way out of this potentially explosive situation other than factual information. It is thus urgent to refrain from formulating too easy extrapolations, if we do not wish to spend the next twenty years with the fear of contamination. Establishing the time lapse during which seropositive individuals are viral carriers is under these circumstances a research priority second only to that aiming at the investigation of the mechanisms of resistance of those who, although infected with the virus, do not develop the full-blown disease.

However, perhaps the first priority is to inform the lay public so that the fear of the unknown does not develop into hysteria, and instead of promising vaccines, which we do not yet know how to produce, it is urgent to explain what AIDS is not and, by

extrapolating from the known, define the limits of the epidemic rather than the boundaries of terror in our imagination.

DIMITRI VIZA

Faculté de Médecine,
Laboratoire d'Immunobiologie,
15, rue de l'Ecole de Médecine,
75006 Paris, France

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What is life?

SIR—R.L. Hoult (*Nature* 316, 480; 1985) is brave to make a stab at clarifying what is meant by saying that a human embryo is "alive".

However, his attempt at distinguishing between dependent and independent viability — with embryos being dependently viable — is not very useful since the word viable means "capable of living either dependently or independently". Hence the problem of defining the words "alive" or "capable of living" is still not addressed in his letter.

The fundamentalists who seek to prevent embryo experimentation may not be impressed, in any case, by a distinction between dependent and independent viability.

The real need is for biologists to seek to change the terms of the debate on experimentation. The problem is that the argument that "embryos are not alive — in some sense or other" is purely defensive. And it is liable to be dismissed for seeking to blind the public with science.

At the root of the debate is a very serious question: "At what point should biologists and others stop seeking to improve the human condition?" Society has views and concerns about this question, as do biologists.

There is probably, for example, general concern that embryo experiments should stop at the point where there are feelings of pain in the embryo. That concern can only be addressed by biologists explaining vigorously and clearly what those words mean and what are the limits of current knowledge on pain in an embryo.

Since the fundamentalism of Darwin's days, the consensus view of society has shifted. Further shifts are likely if biologists are successful in explaining fully and clearly what they are up to, if they demonstrate honestly how their work seeks to improve the human condition and if they win the resources needed to do that job of explaining.

M.A.R. YUILLE

3a Halesworth Road,
London SE13 7TJ, UK

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Good news for Spanish scientists

SIR—Alfonso Martínez Arias's recent letter (*Nature* 18 July, p.184) casts very serious doubts on the attitudes of the Spanish government to reincorporation into the scientific community of young scientists working abroad. I should like to report on recent steps that show, in my view, a much more serious commitment by our government than that conveyed by the statement of your correspondent on "national propaganda (words and wishes)".

First, special fellowships (of which 105 were awarded in August) have been created to help to reabsorb into the Spanish scientific community young researchers who have been working abroad. PhD degrees from foreign institutions are now automatically accepted.

Second, a programme was launched in 1984 to provide funding for both foreign and Spanish scientists intending to spend their sabbatical leave in Spain. Particularly in the case of Spaniards, this may lead to more permanent employment.

Third, in a recent programme for promoting young Spanish scientists to posts in universities and national research laboratories, credit has been given for time spent in foreign institutions. Last but not least, the present government's Law of University Reform has abolished, as a method of university recruitment, those peculiar endurance tests ("oposiciones") that brought so much misery and retardation to Spanish science.

Bureaucracy is, however, always present. Even if some of the statements by Alfonso Martínez Arias about PhD validation are grossly exaggerated, there is undoubtedly ample room for improvement. We are currently working on eliminating obstacles on the basis of the Law of University Reform.

Whether the actions I describe will break all the barriers above the Pyrenees I do not know. These mountains look at times frightfully high. Let us hope, at least, that we shall succeed in tunnelling through them.

J. M. ROJO

Secretary of State for Universities
and Research,
Serrano, 150, 28006 Madrid, Spain

Three of a kind

SIR—You refer to the University of New South Wales as "Sydney's other university" (*Nature* 316, 196; 1985). Actually there are three universities in Sydney. The University of Sydney provides a third option for students, and some very creditable research still goes on there.

MARK WESTOBY

School of Biological Sciences,
Macquarie University,
North Ryde, NSW 2113, Australia

Paradigm still incompletely broken

The centenary of the birth of Niels Bohr next month is both a mark of a milestone past and a reminder that a supposed revolution is incomplete.

IN the customarily over-simple accounts given by sociologists of the development of science, the revolution that was quantum mechanics was eminently one of those occasions when an established orthodoxy, previously defended to the death by diehards, was seen to be untenable, and was abandoned. There was a paradigm shift or, as the sociologists would say, a paradigm shift occurred. The occasion of the centenary of Bohr's birth on 7 October should be a reminder to all concerned that quantum mechanics does not fit this simple description. The paradigm has indeed shifted, but the process took at least the first quarter of this century (a whole working generation) and even now it is incomplete.

The problem is nicely illustrated by the question of who put quantum mechanics on the map. There is an embarrassingly long list of candidates for the distinction, among whom Max Planck is the first: in 1900, he used a simple but ingenious thermodynamic argument to show that black-body radiation must obey Stefan's law that the intensity is proportional to the fourth power of the absolute temperature. He went on to deduce a relationship for the frequency-distribution of black-body radiation (with temperature as a parameter) by an argument which assumed that the total energy of a cavity filled with radiation is distributed among an infinite number of oscillators of different frequency (standing for the possible frequencies of the radiation) only in multiples of some finite amount. The procedure was necessary to avoid trouble with the consistent definition of small quantities, but having started with an assumption denying classical mechanics, Planck and his contemporaries should not logically have been surprised that his result implies that energy is transferred only in quanta of energy, the familiar $h\nu$.

There was some casuistical hand-waving at the time, suggesting that non-classical behaviour applied only to the emission and absorption of energy by the constituents of the walls of the radiation cavity, not to the radiation which filled it.

What mattered was that the result appeared to be correct, in contrast with the classical result suggesting that the frequency distribution of black-body radiation should be an exponentially decreasing function of frequency, or that the Sun should not shine.

Einstein is the next obvious candidate inventor of the quantum theory, chiefly on the strength of not having pedantically picked holes in Planck's shaky calculation but, instead, carrying the implications of Planck's results to their logical conclusion. If radiation consists of quanta, as Newton

IMAGE
UNAVAILABLE
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had once said in different language, then the puzzling production of photoelectrons from metal surfaces became explicable: each would carry off an energy equal to the quantum energy (less the threshold energy), while the number of electrons would be determined simply by the intensity of the radiation.

Again the argument was a direct assault on classical mechanics. People lived with the paradox because the result squared with observation. But perhaps more easily because there were then so many other strange things known, the proof that atoms are not immutable but that they may be radiative chief among them.

Bohr in this spurious pecking-order comes third in time, and perhaps a poor third because his result was so soon shown to be incomplete. By 1913, Rutherford's model of the atom was widely accepted, on experimental grounds, but the stable circulation of electrons around atoms

when, if Maxwell and Lorentz were correct, they should be radiating energy, was only more grudgingly acknowledged to be a fact and — perhaps even more important — Bohr had spent the last six months of the previous academic year with Rutherford at Manchester.

What happened next is legend. Bohr's quantum theory of atoms may now be banished from the textbooks, but it should not be forgotten. It embodied two separate assaults on classical mechanics — a quantum condition that determined which of all circular orbits of electrons around a nucleus may be occupied and the notion that the frequency of the radiation emitted on the transition of an electron from one state to another is the difference of energy divided by Planck's constant, which was a subversive view to take. (Why, it was asked, should not the frequency be related to one or other or even both of the frequencies of revolution of the electron around the nucleus in the first and second states?).

The clinching arguments were the recovery of the empirical formula for the frequencies of the spectral lines of hydrogen due to Balmer thirty years earlier, the accurate calculation of Rydberg's spectroscopic constant in terms of elementary quantities (including Planck's constant) and the successful demonstration that a sequence of observed spectral lines attributed to hydrogen rightly belonged to ionized helium (see *Nature* 4 September, p.5; 1913, and subsequent correspondence).

So, if quantum mechanics was indeed a revolution, 1913 was the year in which it happened. Einstein's discussion of the photoelectric effect had sharpened the dilemma of the duality between light waves and quanta, but nobody could calculate from that starting point the quantities previously unmeasured. There is no point at this stage in asking who played Marx to whose Lenin (or whether Planck was Engels).

From that point on, the log-jam was broken. Sommerfeld rushed off to calculate non-circular orbits, winning much success but quickly meeting awkward discrepancies. Bohr himself sought to account for the splitting of spectral lines by magnetic and electric fields (Zeeman and Stark respectively), again with mixed success. No doubt, if it had not been for the distractions of the First World War, the frailties of the theory would have been

Niels Bohr — Mary Evans Picture Library

Biological manuscripts

Contributors are reminded that, with the transfer of the Biological Sciences Editor of *Nature* to the Washington office, they should in future send **four copies of all manuscripts** to be considered for publication either (as at present) to the London office or to Washington.

revealed more quickly. Bohr himself was conscious of the difficulties. In a lecture to the Danish Physical Society at the end of his *annus mirabilis*, he acknowledged that while these considerations conflict with the admirably coherent group of conceptions which have been rightly called classical electrodynamics, he hoped that by emphasizing the conflict, it may be possible in the course of time to discover a certain coherence in the new ideas. Events have since shown much but not all of what is missing.

None of this, it goes without saying, affects Bohr's stature. It is surely a great strength to be able to regard one's triumphs coolly, and to know how they must be improved. Bohr's own principal concern, for much of the rest of his working life, was to understand the meaning of quantum mechanics. But the chief reason why his centenary is being widely and enthusiastically celebrated is that he acted as midwife for almost all the development of quantum mechanics in the succeeding quarter of a century.

Bohr's achievement as a perpetual group-leader is staggering. It is easier to list those who did not spend much time at Copenhagen (Dirac and Wigner, say) than to list those who did — Ehrenfest, Heisenberg, Gamow, Landau and Pauli among them. Bohr's strong suit, by common consent in the memoirs of the period, was a stubborn determination to get to the bottom of difficult questions. Heisenberg (in *Niels Bohr*, ed. S. Rozental: North-Holland, 1967) tells a half-cruel story of how Schrödinger, soon after the publication of his wave mechanics in 1926, was made so despondent by Bohr's probing that he took to his sick-bed pursued by Bohr, insisting that wave mechanics embodied all the uncertainties by then familiar.

For all that, Bohr's relationship with his junior colleagues seems to have been extraordinarily generous. To improve another's intended publication by constructive argument did not make one a co-author. Heisenberg's first account of the uncertainty principle, the Copenhagen-style Gedanken experiment in which photons and an optical microscope used to measure the position of an electron are found to make the momentum uncertain, appears to have been one of these. But there is also a sad case on record of how Bohr and Kramers, his assistant at the time, jockeyed the then young US physicist J.C. Slater into putting his name on a paper (with them) which implied that energy is conserved only on the average, a notion which did little but cause confusion.

By this time, everything had changed. De Broglie's almost pictorial account of the duality between the wave and particle properties of the electron (1924) was both stimulating and provoking Dirac's abstract but clarifying language for describing the states of quantum systems and the

relationship between them was taking shape. In quick succession (looking back) came Heisenberg's matrix mechanics, and Schrödinger's wave mechanics, essentially the same statements in different language. Electron spin was recognized as such by Uhlenbeck and Goudsmidt (in 1924) and then made sense of by Pauli, who won his exclusion principle as a by-product. Early in the 1930s, people were writing textbooks explaining how to use quantum mechanics as a tool for doing what had eluded Bohr only a little earlier. Pauling and Wilyon's splendid textbook *The Principles of Quantum Mechanics* at that time gave a whole generation of chemists the impression that quantum mechanics was a lode worked out. Those who think the revolution was complete, including some of the practitioners of the times, base their conclusion on the euphoria of the times.

Throughout this period, the memoirs say, Bohr's obsession was with the most difficult of all the difficult questions, that of what quantum mechanics means. There were two successive stages in the argument, the correspondence between quantum and classical mechanics when quantum numbers are large (or if Planck's constant is even smaller than it is) and the degree to which the behaviour of a physical system can be fully described away from the classical limit. These issues are probably still the chief reasons why quantum mechanics remains indigestible, or seems strange. To say that it would be different if there were not such a disparity between the scale on which people ordinarily make observations and those of the atomic phenomena central to the arguments of half a century ago may be true but is unhelpful: the particle phenomena of high-energy physics have a scale almost as many orders of magnitude smaller. But perhaps Bohr should not have been as disapproving as he was said to have been of Gamow's dramatization of the problem in his book about the experience of a man, one Mr Tompkins, who was no bigger than a Bohr radius.

Bohr's distinctive innovation was the doctrine of complementarity, the notion that the outcome of a quantum measurement is conditioned by the construction of the measuring instrument. Put simply, even electrons may exist either as waves or particles, the question of what state they may be in at a chosen time cannot be answered in the abstract because it has no meaning. The issue can be decided only by making a measurement, whereupon the design of the equipment will prejudice the nature of the answer that can be won. Bohr nevertheless consistently fought shy of phrases such as "the observer interferes with the experiment": his view was that the physical system being studied and the instrument used for carrying out the observations are both part of a still larger quantum system.

It is ironical that Bohr's advocacy of this apparently harmless cause should have

brought such controversy on his head. Einstein became a constant critic. Bohr's position was essentially that of a positivist of the school that argued, after Ernst Mach, that the only physical quantities that should play a part in theory are those which can be measured. Which is the view from which Einstein had embarked some decades earlier. Yet Einstein became a fierce critic of Bohr's interpretation. It probably mattered less to Bohr that, in the 1950s, he was labelled by Soviet philosophers as an "idealist", at that time a familiar word of abuse.

The issue over which Einstein and Bohr first fell out, at the Solvay congress in 1927, is still as good an illustration of the difficulty as it was then — take a beam of electrons or photons and direct it at a slit in an otherwise impenetrable screen. Einstein's challenge was that, because of the wave-like character of the entities emerging from the slit, they will spread out in a fan-shaped wavefront. But if the original beam consists of only a single particle, Einstein asked, by what means can the detection of a single particle (electron or photon) behind the screen ensure that the chance of detecting a particle elsewhere on the wavefront is strictly zero?

Bohr's answer lay in complementarity. The act of measurement prejudices the outcome. In the 1930s, Bohr won his battle, although the grumbling from Einstein's school continued, as in Einstein, Podolski and Rosen (*Phys. Rev.* 47, 777: 1935). But that aspect of complementarity which implied correlations between distant parts of quantum systems is still a puzzle, which is why such attention has been given to J. S. Bell's codification of the correlations to be expected in microscopic measurements (see *Physics* 1, 195: 1965). Bell's quantitative test of complementarity has now been verified experimentally, as Bohr would have wished, yet the discussion continues. Some hope to find buried in the complexities of complementarity an explanation of irreversibility in the real world, or of the tendency for entropy continually to increase.

That is one sense in which the quantum revolution is incomplete but there are more obvious difficulties. Gravitation has not been quantized. And while the upheaval that Bohr began has been marvelously successful both as a way of calculating the properties of microscopic systems and as a way of classifying them, the so-called elementary particles, for example, the fact remains that quantum mechanics is a description of the world which is being continually refined. So much is clear from the way in which the subject is taught, as a kind of generalization of classical mechanics. This, again, does not diminish what Bohr and his followers accomplished, but it is a reminder of the dangers of supposing quantum mechanics to be a revolution which is complete. Rather, it is an agenda for a revolution still working its way through physics.

John Maddox

Molecular immunology

Associations in T-cell activation

from Ronald H. Schwartz

WHETHER the T cells of the immune system are in the business of killing infected cells or helping B cells make antibodies, they do so by first recognizing two molecules simultaneously on the surface of the other cell. One is the foreign antigen, for example, a protein produced by a virus; the other is a product of the genes of the major histocompatibility complex (MHC). For 'helper' T cells, which assist B cells in antibody production, the relevant MHC products are known as Ia (or class II) molecules. Most immunologists feel that the T-cell receptor responsible for the recognition process physically contacts both the Ia molecule and the antigen. But it has been hotly debated whether the antigen itself physically interacts with the Ia molecule, either in the presence or absence of the T-cell receptor. On page 359 of this issue¹, Babbitt *et al.* provide a direct answer to this question by demonstrating that an antigenic peptide specifically binds to one allelic form of an Ia molecule and not another. This provides the observation that is needed to understand how Ia molecules can influence T-cell activation in an antigen-specific manner, and suggests that this interaction is one mechanism of immune response (*Ir*) gene control.

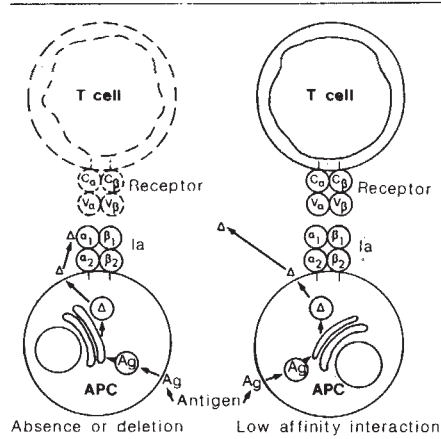
Past controversy has stemmed from the belief that a small number of distinct Ia molecules could not possibly bind in a specific manner the many different antigens that must be recognized by the immune system. Most of the earlier data supporting a physical interaction between antigen and the Ia molecule were indirect. For example, it was shown that T-cell clones capable of recognizing antigen in association with two different Ia molecules display a different pattern of fine specificity of activation with each Ia molecule². And in other experiments^{3,4}, certain antigen analogues that were non-stimulatory were shown to inhibit competitively the activation of T cells by a stimulatory analogue. In neither case, however, was binding measured; the physical interaction was inferred from the effects on biological responses.

In contrast, Babbitt *et al.* have carried out direct binding measurements, using equilibrium dialysis and a fluorescently labelled antigenic peptide, and find a relatively high ($5 \times 10^5 \text{ M}^{-1}$) association constant. One could quibble about the biological significance of this value, as it was determined in the presence of detergent, but the specificity is reasonably convincing. Ia molecules (Ia^k) derived from mice able to respond to the peptide bind at least 10 times as well to the peptide as do Ia molecules (Ia^d) from mice that do not respond (although one would like to see

more than two allelic forms tested in the future). Furthermore, the binding can be inhibited by a 10-fold molar excess of unlabelled peptide but not by a similar amount of a non-stimulatory analogue. Perhaps, an ideal experiment would have included a reciprocal result, in which a second antigen bound to Ia^d but not Ia^k , where mice expressing Ia^d were responders to that antigen and mice expressing Ia^k were non-responders.

Can such interactions explain the phenomenon of *Ir* gene control, which includes the fact that the particular allelic form of an Ia molecule an animal possesses determines the antigens to which the animal can respond⁵? Although the mechanism by which this regulatory control occurs is not understood, two general schemes have been suggested (see figure).

One scheme suggests that the T-cell population is skewed by the presence of



Two schemes to explain how a processed antigen (Δ) on the surface of an antigen presenting cell (APC) may not be recognized by a T cell.

the Ia molecule. This could occur through positive selection of an anti-self MHC recognition repertoire in the thymus, through negative selection during the generation of self tolerance, through the induction of suppressor T cells that are specific for the Ia molecule, or because the germline does not encode T-cell receptor V regions capable of recognizing the Ia molecule in association with the antigen. In each case, a non-responder animal would be one that lacked T cells able to recognize or respond to the antigen in association with that animal's own Ia molecules (left hand side of figure).

The other scheme suggests that the antigen physically interacts with the Ia molecule and either forms a complex for the T-cell receptor to recognize, or stabilizes the interaction between the T-cell receptor and Ia molecule that occurs during T-

cell activation. In either case, non-responsiveness would then be the result of too low an affinity of interaction between the antigen and the Ia molecule (right hand side of figure). Clearly, the experiments of Babbitt *et al.* support the second scheme. They do not, however, preclude the first, since the mechanisms are not mutually exclusive.

What about the problem of the limited diversity of Ia molecules? This becomes a moot point if the same findings can be reproduced with different antigenic peptides. However, at this juncture one can still argue that the observations of Babbitt *et al.* represent an unusual case. An association constant of $5 \times 10^5 \text{ M}^{-1}$ is a modestly high affinity (equivalent to hapten binding by some antibodies), and I think many other interactions will be of lower affinity, in the range of $10^4 - 10^5 \text{ M}^{-1}$. Nonetheless, I see no reason why a set of proteins could not evolve to have generalized weak binding for small peptides, as originally suggested by Benacerraf⁶. After all, serum albumin appears to have evolved as a general transport protein for various unesterified fatty acids and haem derivatives.

Perhaps the confusion lies in the assumption that the Ia molecule alone imparts all of the specificity to the immune response. Undoubtedly the T-cell receptor plays the major role in this specificity but, for reasons that are still not understood, this receptor is forced to recognize Ia molecules in addition to the foreign antigen. If, during this process of dual recognition, the antigen and the Ia molecule are inevitably brought into physical contact, then one could imagine that the Ia molecule has evolved to facilitate this interaction, so generating a structure that is favourably disposed to interact with a variety of different peptides. The Ia molecule is large enough for this to have been achieved by creating distinct substitutes for binding peptides with different chemical properties. Experiments with Ia mutants and inhibition studies with monoclonal antibodies have already provided evidence for the existence of functional subsites on the Ia molecule⁷⁻¹⁰.

Finally, if Ia molecules and antigens do interact physically, another potential problem is the competition from self proteins that must occur as they are processed through antigen-presenting cells (APC in the figure). T-cell clones specific for self proteins can be deleted or inactivated during the induction of tolerance to prevent the animal from responding to itself, but self molecules will still be processed by the antigen-presenting cells and could interact with the Ia molecule, preventing it from binding to a foreign protein. If so, for a foreign protein to be immunogenic would require it to differ in sequence from self proteins in a way that would either yield an antigenic peptide with a greater affinity than processed self proteins for the same site on the Ia molecule, or create a peptide that interacts with a different site

on the Ia molecule.

A possible example of this is the murine immune response to pigeon cytochrome c (ref. 11), where the critical difference between mouse and pigeon cytochromes c lies in the part of the peptide that interacts with the Ia molecule (the agretope). Competition experiments in a binding assay similar to that described by Babbitt *et al.* should be able to discriminate between the two mechanisms — higher affinity or a different binding site — in this particular case. In the more general case of non-homologous self proteins producing peptides that compete for binding at particular Ia sites, it is not clear that having multiple binding sites will totally solve the competition problem. More attention will

have to be paid to this problem in the future, if the experiments of Babbitt *et al.* can be generalized to other antigens. □

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Ronald H. Schwartz is in the Laboratory of Immunology, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland 20205, U.S.A.

Solid state physics

Unravelling disorder in glass

from P. H. Gaskell

WHY do some melts form glasses on quenching whereas others crystallize? A related question concerns the extent of positional and compositional order: is the structure of a glass random beyond nearest neighbours or are there clearly recognizable 'molecular' fragments that would also be evident in the lattice of a compositionally equivalent crystal? These questions are raised and partly answered in a recent paper by D. Ruffolo and P. Boolchand¹ on the structure and glass-forming ability of germanium tin sulphides.

One view of the structure of glasses is that certain local atomic configurations are preferred energetically but possess point-group symmetry which precludes efficient space-filling, and particularly is inconsistent with the requirements of periodicity, so that there may be a bias against crystallization. A macroscopic structure then forms only when the local symmetry is occasionally broken — regular breaks in symmetry may lead to 'quasi-crystalline' solids such as the recently discovered Al-Mn alloys^{2,4}, or to the so-called Frank-Kasper³ structures observed in some truly crystalline intermetallic alloys. If defects are introduced irregularly then a glass may be formed.

Another view is that to avoid crystallization during quenching, the number (and magnitude) of the ordering forces should be small in comparison with the number (and relative stability) of alternative, non-periodic, atomic configurations. The number of such ordering constraints per atom must not, however, be too small in relation to the degrees of freedom: otherwise a disordered fluid state may persist to temperatures well below the liquidus temperature where the probability of crystal nucleation is large and the steady increase in melt viscosity, which leads eventually to the solid-like proper-

ties of the glass, becomes less likely.

How many constraints should there be in relation to the degrees of freedom? Phillips⁶ has made the simple suggestion that the two should be equal for an ideal glass-forming composition. If the number of constraints per atom, N_c , is the dimensionality = 3, the most suitable glass-forming compositions in covalent chalcogenide systems can be picked out in an impressive way. Phillips' condition thus provides a simple link between the connectivity of a network and the dimensionality of the system. The ideas have been extended^{7,8} to plot threshold conditions for a rigid glass-like structure.

There are some difficulties, though, in applying the notions in anything other than a qualitative way. Metallic alloys form glasses but have no obvious network. In SiO_2 , the archetypal glass-forming oxide, some of the weak bending constraints must be ignored. Some melts are thought to consist of randomly linked clusters of well-defined groups of atoms and it becomes necessary to select the 'effective' constraints very carefully.

In relatively complex systems like the germanium tin sulphides studied by Ruffolo and Boolchand, such detailed considerations may be some way off. They have, however, obtained an interesting link between glass-forming ability and the structure of the glass. This relates directly, but as yet only qualitatively, to the notions based on constraints. They have obtained the Mössbauer spectra for Sn in a series of crystalline solids, $\text{Ge}_{2-2x}\text{Sn}_{2x}\text{S}_3$, ranging from SnGeS_3 to Sn_2S_3 . In SnGeS_3 , a corner-sharing network of GeS_4 tetrahedra is coupled laterally through weaker Sn^{2+} -S bonds (Fig. 1a), and the Mössbauer spectrum consists only of a doublet due to Sn^{2+} . In crystals containing more tin, the excess Sn is thought to substitute as Sn^{4+} for Ge and a characteristic Mössbauer peak is

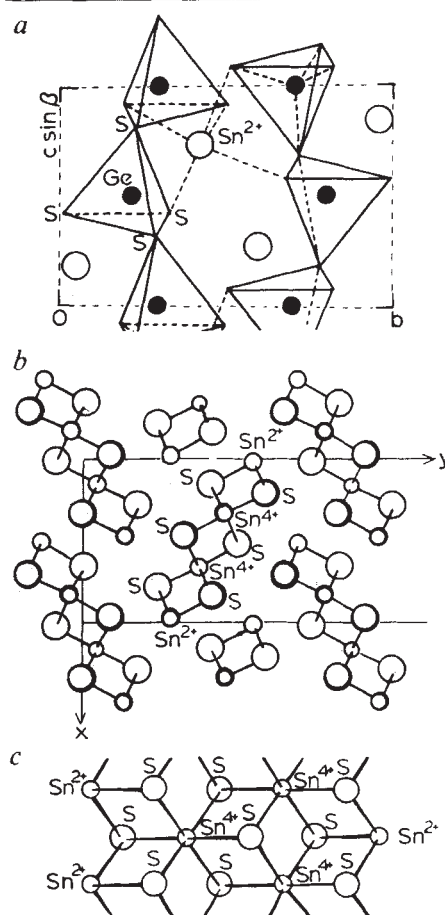


Fig. 1 a, Crystal structure of SnGeS_3 showing the zig-zag chains of corner-sharing GeS_4 tetrahedra that couple laterally (along the b axis) by weaker Sn-S bonds. b, $\text{c-Sn}_2\text{S}_3$ structure which consists of infinitely long, thin and narrow molecular ribbons having their planes along the z axis. c, A lateral view of the ribbons showing Sn^{2+} and Sn^{4+} edge and interior cation sites. (From ref. 1).

observed. Further increases in the Sn content leads to a separation into two phases — SnGeS_3 and Sn_2S_3 . The latter has a structure consisting of thin planar ribbons which couple only through weak Van der Waals forces (Fig. 1b, c). In this crystal Sn^{4+} ions are octahedrally coordinated, giving a typical Mössbauer signature. The change from a lattice in which Sn^{4+} substitutes for Ge in tetrahedral sites to the Sn_2S_3 -type structure with octahedral Sn^{4+} occurs at a well-defined composition $x \approx 0.7$.

Comparison of the Mössbauer spectra of compositionally equivalent crystals and glasses shows close similarities, suggesting an equivalence in structures and thus a change from a structure based on distorted $(\text{Ge}, \text{Sn})\text{S}_4$ units to one similar to the Sn_2S_3 lattice with long molecular ribbons. The authors stress that formation of glasses from the melt also becomes more difficult over the same concentration range, suggesting that the polymeric chains shown in Fig. 1a promote glass formation because of the 'floppiness' of the network, whereas the more rigidly constrained and partially organized Sn_2S_3 planar ribbons do not allow sufficient

variability for glasses to form.

The results, then, represent yet another straw in the wind — the structures of certain glasses may be more closely linked to those of compositionally equivalent crystals than simple theories imply. And if the properties of these glasses can be related to their equilibrium crystalline phase diagrams, where does this leave theories of the structure of glasses based on the non-equivalence of crystallographic and 'non-crystallographic' clusters? □

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P.H. Gaskell is at the Cavendish Laboratory, Madingley Road, Cambridge CB3 0HE, UK.

Membrane channels

Bridging the junctional gap

from Harry Goodall

AMONG transmembrane channels, gap junctions are unique because they link the interiors of adjacent cells (see figure), rather than allowing specific ions to enter from the extracellular medium. As well as their obvious role in providing a metabolic continuum through tissues, there is mounting evidence that groups of cells sharing common developmental or physiological strategies may be preferentially coupled through the gap junctions between them. Consequently, a great deal of attention has recently been directed towards finding out how the conductance of these channels is regulated. On page 331 of this issue¹, Jacques Neyton and Alain Trautmann report the use of one of the most powerful tools in the armoury of the ion-channel investigator, the whole-cell patch-clamp technique, to probe the specificity, the regulation and the conducting ability of the individual channels that make up each gap junction.

Patch clamping, as its name suggests, involves the formation of an extremely high resistance seal between a large-bore (1–2 µm) glass micro-pipette electrode and the cell membrane across its tip. The patch is ruptured so that the interior of the cell is now continuous with the fluid in the pipette, allowing manipulation of the internal environment and clamping of the membrane potential at specific values. Neyton and Trautmann¹ have extended the method to examine pairs of cells from the rat lacrimal gland that are coupled by intercellular junctions. With one patch electrode on each cell, the minute currents passing through individual channels as they open in succession can be measured when the potential in one cell is changed.

As suspected, the channels show little specificity: ions of different species and charge pass through with almost equal ease. Unlike many types of transmembrane channel and indeed some gap junction preparations², the gating of the channels in this preparation is independent of the transchannel voltage; the channel conductance is relatively large, its mechanism slow and its gating symmetrical. What then is the gating mechanism? Generally,

it has been thought that the internal concentration of free Ca²⁺ modulates the junctional conductance (for a mechanism involving the intervention of Ca²⁺ and calmodulin, see ref. 3) but an independent role for intracellular pH has more recently been suggested⁴. Using the improved recording technique, it should be possible to clarify this issue. If, as seems likely, the predominant mechanism varies according to cell type, the subtlety with which gap junction channels are regulated will be very interesting indeed.

The intensity of present investigation into such subtleties was demonstrated amply at a recent EMBO workshop*. Much new data, some of it preliminary, were presented, obtained by a combination of established and innovative techniques on a variety of cell types. Traditional methods such as plotting the spread of injected dyes across the boundaries between coupled cells now are being analysed quantitatively by S. Caveney (University of West Ontario) and P.R. Brink (State University of New York, Stony Brook) so that the constraints to and regulation of diffusion can be assessed. J.D. Sheridan (University of Minnesota) has used this approach to show that junctional defects may be closely associated with the process of cell transformation.

Sheridan's method of producing transformed cells, by using a temperature-sensitive virus that introduces a protein kinase, may also provide a pointer to the identity of the process regulating channel conductance. R.G. Johnson (University of Minnesota), E.L. Hertzberg (Baylor College of Medicine, Houston) and K. Willecke (University of Essen) showed that isolated junctional protein could act as a substrate for phosphorylation when incubated with cyclic AMP or protein kinases such as, tantalizingly, protein kinase C. This implies that junctional regulation may dovetail into the greater complexities of cellular control⁵.

It is not yet clear whether there is more

than one type of gap junction. The junctions between epithelial cells and those between the fibre cells of the eye lens seem to behave differently to an uncoupling stimulus (D.A. Goodenough, Harvard Medical School), although this could reflect regulatory differences between the cells. Nevertheless the cell or tissue specificity of the junctional protein is a continuing source of discussion. Cloning and subsequent identification of the primary sequence of the lens junction protein by J.-P. Revel and his colleagues (California Institute of Technology, Pasadena) indicates that, although there is no sequence homology with junctional material from other tissues, the predicted quaternary structures correspond well. This may well allow antigenic differences between junctions from different tissues even though structural constancy is maintained.

This is the area of greatest controversy in the subject because a useful way to investigate the function and control of junc-

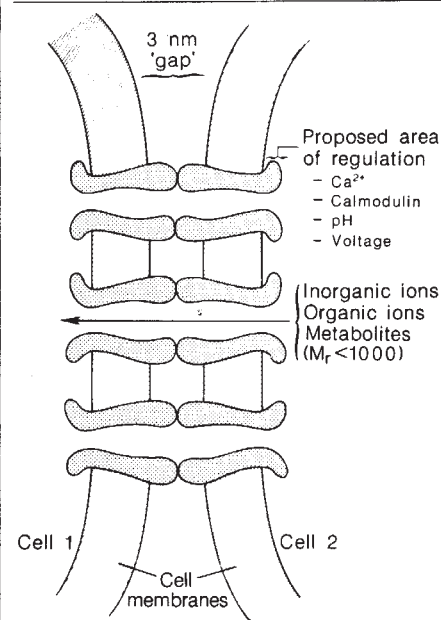


Diagram of a section through a gap junction. In specific areas of apposed membrane, channels lined by six protein subunits⁵ are sealed to their counterparts and link the cytoplasm of both cells. These channels allow transcellular passage of ions and metabolites of molecular mass less than 1,000 (approximately 1,800 in arthropods) and are common to most tissues⁶.

tional coupling should be to raise antibodies against the protein and use them to block or modify junctions *in situ*. Indeed, some success was reported, most impressively the ability to interfere with the maintenance of head-axis integrity in *Hydra* (N.B. Gilula, Baylor College of Medicine) and with specific cell lineage in *Xenopus* (A.E. Warner, University College London).

The outstanding difficulty in all these studies is that antibodies are raised to isolated junctional membranes rather than to a single protein. Unfortunately the only method available for assessing the purity

*The European Molecular Biology Organization workshop on "Structure, Regulation and Function of the Gap Junction" was held at the Station Biologique, Roscoff from June 23–27, 1985.

of isolated junctions is to examine them under the electron microscope and then to monitor their composition using SDS-polyacrylamide gel electrophoresis. Gilula emphasized that some antibodies, apparently specific to junctional membrane, appear to be localized to closely associated extracellular material; similarly, Goodenough showed that an antibody, apparently specific to junctional protein, bound only to non-junctional membrane.

Given these uncertainties, it is not entirely surprising that there are now two candidates for the junctional protein. Isolated junctional membrane contains a series of related proteins with relative molecular masses ranging from 10,000 (10K) to approximately 70K. The 27K protein (26K in the lens) has usually been assumed to represent the fundamental subunit of this channel. J.D. Pitts, M.E. Finbow and colleagues (Beatson Institute for Cancer Research, Glasgow) using a modified extraction procedure have, however, produced an entirely new contender with a molecular weight of 16K. This protein has little or no homology with the 27K protein but is structurally related to an analogous 18K protein from

arthropods. A state of impasse now exists, revolving around the fact that antibodies to the 16K protein perform all the same feats as the antibodies to the rival 27K protein.

Perhaps this problem will be resolved through approaches such as that of H. Evans (National Institute of Medical Research, London), who has generated antibodies against synthetic sections from identified sequences in the junctional protein. Ultimately, the cloning approach of Revel and his colleagues, followed by the generation of ultra-specific probes and reconstitution of positively identified material into model membranes should provide the answers. The momentum that has now been generated will certainly ensure that there is no shortage of activity over the next few years. □

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Harry Goodall is in the Department of Anatomy, University of Cambridge, Downing Street, Cambridge CB2 3DY, UK.

Cosmology

Heavy neutrinos and galaxies

By N.A. Jelley

DO HEAVY neutrinos exist, and if they do what are the implications for the formation of galaxies? On page 335 of this issue, T. Padmanabhan and M.M. Vasanthi discuss the cosmological implications of heavy, unstable 17 keV neutrinos and come to the conclusion that it is very difficult to accommodate such neutrinos into the standard model of the Universe. This fits in very well with the latest conclusions from particle physics which, as discussed in these columns last week (12 September, page 107), also deny the existence of a 17 keV neutrino.

This flurry of interest in heavy neutrinos has arisen from the result recently published by J.J. Simpson² of an experiment that revealed a kink in the electron energy spectrum for tritium β decay. This is not what would be expected in the usual picture of β decay, where a light neutrino (with a mass less than about 50 eV) is emitted together with the electron. It has been speculated that there is a small probability of a heavy neutrino being emitted in β decay. One consequence of such a hypothesis is that there would be a small kink in β decay spectra, just like that reported by Simpson. The position of the kink determines the neutrino mass, and Simpson interpreted his results as evidence for a heavy neutrino of about 17 keV mass. This has already led to some interesting speculations^{3,4} as well as giving

impetus to the work by Padmanabhan and Vasanthi.

Massive neutrinos have often been suggested as possible candidates for the dark matter or 'missing mass' in the Universe. As this material cannot be seen, its existence has been inferred from studies of the motion of stars within galaxies and of galaxies within clusters. These indicate that the mass of dark matter is an order of magnitude greater than that of visible material. Cosmological estimates of the number of neutrinos have shown, however, that a stable massive neutrino must have a mass less than about 200 eV or greater than about 200 MeV; otherwise the predicted neutrino mass density would exceed the current estimates of the density of the Universe. Thus a 17 keV neutrino would have to be unstable.

Padmanabhan and Vasanthi¹ find that an unstable 17 keV neutrino does not give rise to any contradictions with the observed age or density of the Universe. But they reach the interesting conclusion that the decay products from such a particle would wash out the inhomogeneities in the early Universe necessary for the formation of the galaxies we see today.

But if they do not provide the dark matter in the Universe, then what does? There have been many suggestions including black holes, faint stars, planets and rocks, as well as more exotic undis-

covered particles like axions, photinos and magnetic monopoles. There are problems with most known particles (see ref. 5), though the light neutrino is still a possibility. In a series of experiments on tritium β decay, a group at ITEP, Moscow, have concluded^{6,7} that the neutrino has a mass of 33 eV, and could therefore account for the dark matter. Such a mass is near the limit of what can be measured with present experimental techniques and there are several groups throughout the world (see ref. 8) trying to check this result. Even if it were confirmed there could still be difficulties in the standard model, as it has been argued that even a light neutrino would make it hard to understand the formation of galaxies⁸.

Failing neutrinos, what is left? Of the other candidates for dark matter, axions are in favour at the moment. These particles were originally proposed to avoid predicting large symmetry (charge-parity) violations in the strong interaction, which are not observed. Axions must interact very weakly with matter and so would be very difficult to detect. Experiments have been proposed⁹ but there are no results as yet. Another possibility, though less favoured as a candidate for the dark matter, is the magnetic monopole. This particle is predicted by various grand unified theories and there are several groups currently trying to detect a monopole¹⁰. There are also several experiments underway at particle colliders that have so far provided the only limits on the mass of several candidates, including the photino¹¹.

Now the results from the particle physics experiments aimed at checking Simpson's interpretation have become known. Altitzoglou *et al.*¹² conclude there is no evidence from the decay of ³⁵S for the presence of 17 keV neutrinos. Moreover, Haxton¹³ has decided it is plausible that a careful treatment of atomic effects will provide a conventional explanation of the observed kink in the tritium β decay spectrum.

It would thus appear that the great difficulties over the existence of a 17 keV massive neutrino pointed out by Padmanabhan and Vasanthi will not have to be faced. Their paper is another powerful demonstration of the close links between the apparently unconnected fields of particle physics and cosmology. □

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N.A. Jelley is a Lecturer in the Department of Nuclear Physics, Keble Road, Oxford OX1 3RH, UK.

Pollination mechanisms

Exploitation of animal mobility

from Peter D. Moore

CO-EVOLUTION of plants and insects, particularly in terms of pollination, is full of subtle and striking relationships. In the palms, for example, the mechanism of pollination varies between species and for some palms uncertainty still exists about the relative importance of wind and various insects in effecting pollen transfer¹. The blueberries (*Vaccinium* spp., Ericaceae) are clearly insect pollinated, but a recent report suggests that a pathogenic fungus also uses the insects for transport from one plant to another². Great selective advantages are evidently associated with the development of mechanisms that exploit the mobility of animals to disperse pollen grains and spores.

In his work on palms, J.H. Beach has examined the reproductive biology of two species of *Bactris* in the lowlands of Costa Rica¹. Palms generally produce very large quantities of pollen, a feature often associated with wind pollination; but recently many palm species have been found to rely on insects, which may explain why palms are so poorly represented in the current pollen rain of the Mediterranean

odour that is emitted is accompanied by the heating up of the inflorescence, which probably serves to volatilize the scented compounds⁴. The female flowers on the spike are receptive and the whole inflorescence is soon invaded by weevils 2 millimetres long and then by scarab beetles 2 centimetres long. The weevils gather in very large numbers, up to 100,000 per inflorescence, and feed on the outer parts of the petals of the male flowers, which are conveniently free of the tannins found in other floral parts.

The scarabs also gather in thousands and indulge in two main activities: copulation and extensive feeding on knobbed hair structures found on the inflorescence stalk. The shelter and relative safety of the palm inflorescence for copulation may be one of its main attractions, as Beach has previously observed in other flowers, such as *Cyclanthus*⁵. The feeding activity on the hairs, however, is surprising because they pass through the gut structurally unaltered. Evidently the hairs are not a major energy resource, but they could supply some other dietary requirement.

It is not yet clear which of these two potential pollen vectors is the more efficient. But because the inflorescence contains dietary resources that are attractive to both insects, each vector possibly provides advantages for specific conditions, such as different inter-tree distances⁵.

The studies of Batra and Batra² on blueberries, on the other hand, provide

the first observation of a pathogenic microbe that has evolved a sophisticated form of mimicry to take advantage of pollination vectors moving between plants as a means of spore dispersal. The fungus *Monilinia* spp. infects *Vaccinium* species and *Gaylussacia baccata* (huckleberry) in North America, causing the development of withered 'mummified' berries in which the fungus overwinters. Young shoots are infected in the spring and become discoloured and wilted. These shoots are coated with a layer of conidia rich in sugars, which attracts the attention of insects engaged in floral foraging. But what the insects find most attractive is the ultraviolet reflection from the wilted leaves, which corresponds to that of the *Vaccinium* flower calyx. Evidently this acts as a honey guide under normal conditions, a form of flower mimicry by a fungus that has never been recorded previously.

The efficiency of the mechanism for spore dispersal was tested by excluding insects from 400 flowers and pollinating them by hand. The bags used for insect exclusion allowed air currents to pass through, along with any suspended fungal spores. Of the resulting fruit produced, only 10 per cent were infected compared to 63 per cent under control conditions. There seems to be no limits to the subtleties evolved by the plant and microbial kingdoms to harness mobile animals for their own ends. □

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Peter D. Moore is Reader in Ecology, Department of Biology (KQC), King's College, 68 Half Moon Lane, London SE24 9JF, UK.



Scarab beetles feeding on an inflorescence of the peach palm (*Bactris gasipaes*).

area³. Few detailed observations have been made, but Beach has documented the course of events in *Bactris gasipaes*, a cultivated species and the wild *B.porcschiana*. The *Bactris* inflorescence, or flower cluster, is a mass of spikes (see figure) that pushes its way out of an enveloping bract late in the afternoon. No nectar is produced, but the musky

Human reproduction

Prospects for developing vaccines to control fertility

from G. L. Ada, A. Basten and W. R. Jones

SINCE its establishment in the early 1970s, the World Health Organization's (WHO) special programme of research, development and research training in human reproduction has been engaged in the development of new and improved methods of fertility regulation*. The need for these studies, being carried out at the request of the governments of several developing countries, is as great now as it was at the outset of the programme. There are thought to be six hundred million couples of reproductive age in the developing countries; some eighty per cent of these, for various reasons, do not use adequate methods of birth control.

One new approach that could yield an efficient, safe and cheap method is a fertility-regulating vaccine. In April 1985, an expert panel at WHO reviewed progress in defining reproduction-specific antigens which could be used in the development of such vaccines; the criteria that these antigen(s) should meet; and the application of new technologies in the detection and study of appropriate antigens.

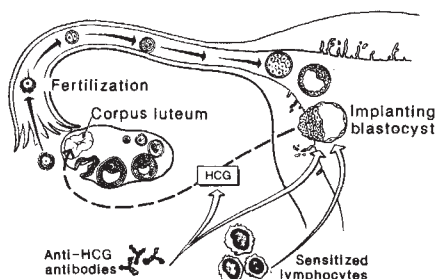
The following factors are relevant in selecting target antigens for acceptable fertility control vaccines. The antigen should be: (1) present transiently and in low amounts relative to the predicted antibody response (sequestered antigen not excluded); (2) specific, that is, restricted to the target; (3) chemically well characterized to facilitate manufacture by modern

*WHO Special Programme of Research, Development and Research Training in Human Reproduction 13th Annual Rep. (1984).

techniques; (4) restricted to gametes and/or the early products of fertilization (full functional characterization of the antigen being desirable, but not essential).

To be acceptable, the vaccine should have an efficacy rate of at least 90 per cent; elicit a reproducible immune response of the desired magnitude, nature and duration, irrespective of genetic background and health/nutritional status of recipients; be free of side-effects; exert an anti-fertility effect which is potentially reversible, either spontaneously or by manipulation; and be suitable for widespread use. To satisfy many of these requirements, safety and efficacy testing in an appropriate animal model is necessary before the initiation of human studies.

A decade ago WHO decided to coordinate and sponsor the development of a vaccine which was based on the carboxy-terminal polypeptide of the β subunit of human chorionic gonadotrophin (hCG).



Possible modes of action of anti-hCG vaccine. Antibodies capable of neutralizing hCG may inhibit its luteotrophic action on the corpus luteum. Cytotoxic anti-hCG antibodies or sensitized lymphocytes may disrupt the early peri-implantation blastocyst (reproduced from Jones W.R. *Immunological Fertility Regulation*, Blackwell Scientific, Melbourne, 1982).

a protein hormone produced by the early trophoblast. One of the functions of this hormone is the maintenance of progesterone production by the corpus luteum in a conceptual cycle (see figure). Abrogation of this role by vaccination mimics physiological luteolysis and results in menstruation, thereby preventing pregnancy in what otherwise seems to be a normal non-conceptual menstrual cycle. A prototype vaccine on which preclinical toxicity and safety evaluations have already been completed is now ready for clinical testing. It is a multicomponent formulation consisting of (1) an oligopeptide corresponding to the amino-acid sequence 109–145 of the carboxy-terminal region of the β subunit of hCG; (2) a protein carrier, diphtheria toxoid, to which the oligopeptide is conjugated; (3) a synthetic adjuvant based on muramyl-dipeptide which seems to be as potent as the clinically unacceptable Freund's complete adjuvant, but without the ability of the latter to generate extensive tissue reactions.

The peptide-carrier conjugate and adjuvant are suspended in saline and emulsified with arlacel A in squalene. Active immunization with this preparation has

been effective in inhibiting fertility in baboons (Stevens, V.C. *et al. Fertil. Steril.* 36, 98; 1981), even though there is only 3–15 per cent cross-reactivity between antibodies to the carboxy-terminal region of hCG and baboon CG. Toxicity studies in rodents, rabbits and baboons have failed to demonstrate any adverse side-effects of this treatment and extensive screening of immunized baboons has failed to reveal significant titres of auto-antibodies or evidence for immune-complex deposition in tissues. On the basis of these encouraging results, WHO plans to carry out a clinical trial to assess the immunological efficacy and safety of the vaccine as soon as approval from regulatory authorities has been obtained. At the same time, work has been progressing on the synthesis of the corresponding oligopeptide from baboon CG to allow further studies with a baboon CG vaccine that will more closely approximate to the clinical situation in which the hCG vaccine will be used.

During the past decade significant progress has been made in the search for additional vaccine candidates. Sperm antigens comprise one possibility for both males and females, as they are present only transiently in the female reproductive tract and are sequestered in the male, where their expression is restricted to testicular germ cells and sperm. Immunization of females with whole sperm or two preparations of isolated sperm antigens — the sperm-specific enzyme lactate dehydrogenase (LDH-4) and a germ-cell antigen (GA-1) derived from spermatocytes — has been effective in reducing fertility in animals. Such studies, together with evidence of anti-sperm antibodies in healthy but infertile men and women and vasectomized men, suggest that naturally occurring sperm antibodies with adequate anti-fertility properties have no deleterious effects on the host. In animals, fertility, has returned after sperm antibody titres waned. Of the sperm antigens identified to date, only LDH-4 has been well defined; however, it should be possible to produce this and other suitable polypeptides by modern techniques. In the female, access by antibodies to the target may be a problem and further consideration should be given to the use of mucosal as well as systemic routes of immunization.

Immunization with well-characterized zona pellucida (ZP) antigens can inhibit fertility in several species. Some antibodies to ZP glycoproteins inhibit sperm-ZP interaction *in vitro* (both binding and penetration). However active immunization with ZP seems to result in an unacceptable alteration in ovarian function. Whether other ZP antigens can elicit anti-fertility antibodies without such side-effects must be determined before such antigens become candidates for vaccines.

Trophoblast surface antigens have the

100 years ago

ADDRESS BY FRANCIS GALTON, F.R.S., ETC, President of the Anthropological Institute.

THE object of the Anthropologist is plain. He seeks to learn what mankind really are in body and mind, how they came to be what they are, and whither their races are tending; but the methods by which this definite inquiry has to be pursued are extremely diverse. My data were the Family Records entrusted to me by persons living in all parts of the country, and I am now glad to think that the publication of some first-fruits of their analysis will show to many careful and intelligent correspondents that their painstaking has not been thrown away. As the popular views of what may be expected from inheritance seem neither clear nor just, the subject of my remarks will be "Types and their Inheritance." I shall discuss the conditions of the stability and instability of types, and hope in doing so to place beyond doubt the existence of a simple and far-reaching law that governs hereditary transmission, and to which I once before ventured to draw attention, on far more slender evidence than I now possess. My experiments have shown that the mean filial regression towards mediocrity was directly proportional to the parental deviation from it. from *Nature* 32 507, 24 September 1885.

advantage of being expressed only at one anatomical site following fertilization and of being in intimate contact with maternal blood at a very early stage in pregnancy, perhaps within 10 days of ovulation in the human. Studies with human tissues indicate the existence of potentially suitable tissue-specific and possibly stage-specific cell-surface antigens, but a relevant animal model for efficacy studies is required.

Embryonic antigens, some carbohydrate, are transiently expressed in low concentration on early embryonic cells in several species. As they may also be present in sperm, antibodies specific to them could have two targets. The pattern of temporal expression of these antigens in the embryo needs to be established before this target satisfies the criteria of a vaccine antigen.

Based on data already available, together with the rapidly expanding potential of recombinant DNA technology and other techniques of molecular biology using synthetic vaccines, an appropriate iso-immunogen has considerable promise for the development of a safe, effective and cheap fertility-regulating vaccine. There is, therefore, an urgent need for further research, particularly because of the probability that the user population will increase if vaccination against common infectious diseases in the developing world is successful. □

G.L. Ada is in the Department of Microbiology, John Curtin School of Medical Research, Australian National University, Canberra, ACT, Australia; A. Basten is at the Clinical Centre, University of Sydney, Sydney, NSW, Australia; W.R. Jones is in the Department of Obstetrics and Gynaecology, Flinders Medical Centre, University of South Australia, Bedford Park, SA, Australia.

Mathematical topology

Solving a knotty problem

from Ian Stewart

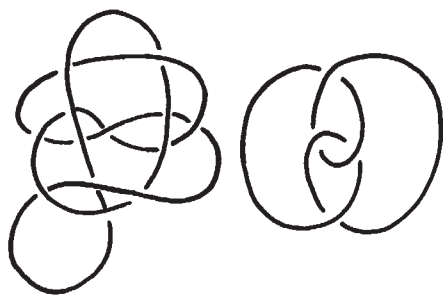
OCCASIONALLY scientific discoveries are made simultaneously by several different people. In topology, an extreme case occurred recently, and is described as follows in the *Bulletin of the American Mathematical Society*. "The editors received, virtually within a period of a few days in late September and early October 1984, four research announcements, each describing the same result — the existence and properties of a new polynomial invariant for knots and links. There was variation in the approaches taken by the four groups and variation in corollaries and elaboration. These were: *A new invariant for knots and links* by Peter Freyd and David Yetter; *A polynomial invariant of knots and links* by Jim Hoste; *Topological invariants of knots and links* by W.B.R. Lickorish and Kenneth C. Millett; and *A polynomial invariant for knots: a combinatorial and an algebraic approach* by A. Ocneanu. It was evident from the circumstances that the four groups arrived at their results completely independently of each other, although all were inspired by the work of [Vaughan] Jones . . . The degree of simultaneity was such that, by common consent, it was unproductive to try to assess priority. Indeed . . . there is enough credit for all to share in."

As a compromise, all six authors combined together to write a paper (*Bull. Am. Math. Soc.* 12, 239; 1985) stating their common main result and explaining each group's particular viewpoint. Curiously, there are considerable differences in the proof and the point of view adopted. The new invariant is simple and powerful, and it is surprising that it has eluded topologists for so long.

To a topologist a knot is any simple closed curve embedded in three-dimensional space. Two knots are (topologically) equivalent if there is a continuous transformation of the surrounding three-dimensional space that carries one knot to the other. Similarly, a link is a finite set of simple closed curves, with an analogous definition of equivalence. The main problem is to decide whether two

given knots or links are equivalent, and this is generally approached by using the idea of a topological invariant. This comprises some mathematical data (usually of a combinatorial or algebraic character) associated with each knot in such a way that equivalent knots have the same data. Thus knots with different data cannot be equivalent but knots with the same data need not always be equivalent.

The first effective invariant was found by Hans Reidemeister in the 1920s, and it enabled him to give the first rigorous proof that knots exist. His invariant can be described in terms of the knot diagram, which is just a picture of the knot in which all crossings are neatly separated from each other and with a small gap drawn in the lower strand of each crossing, much as a road map shows a bridge. Pretend that this gap is real — the knot then splits up into several components; at each crossing one component forms the overpass while

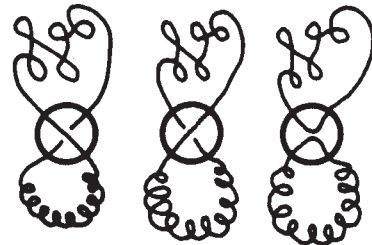


two others form the underpass. Say that the knot can be n -coloured if it is possible to assign to each component a number $0, 1, \dots, n-1$ in such a way that: (1) at least two components have different numbers; and (2) at each crossing the sum of the numbers on the two underpass components is equal to twice the number on the overpass, up to a multiple of n .

Then, by analysing how deformations of the knot alter its diagram, and thus affect colourability, it can be shown that the set of integers n for which a given knot is n -colourable is an invariant. An ordinary overhand knot is 3-colourable but not 5-colourable; a 'figure of eight' knot is 5-colourable but not 3-colourable; and an unknotted loop is not n -colourable for any values of n . Hence all three are different.

A more sophisticated invariant, the Alexander polynomial, associates with each knot or link K a polynomial in one variable t . For the trefoil it is $t^2 - t + 1$, and for the figure eight $t^2 - 3t + 1$. Again the invariant is good enough to distinguish the two. John Conway (*Computational Problems in Abstract Algebra* 379; Pergamon, Oxford, 1970) developed a method for computing Alexander polynomials based on a relation between the Alexander

polynomials of a given link K and two modifications of it, L and M . L is obtained from K by taking a single crossing and changing the overpass to an underpass; M is obtained by cutting both strands at the crossing and joining them in pairs so that they do not cross at all. Vaughan Jones (*Bull. Am. Math. Soc.* 12, 103; 1985) applied the theory of Van Neumann algebras



— a topic in functional analysis — to derive a new knot polynomial, also in one variable, satisfying a very similar relation.

The latest invariant can be considered either as a homogeneous polynomial in three variables or as an inhomogeneous polynomial in two. In terms of three variables it is the unique such function P on (equivalence classes of) knots such that:

$$(1) xP_K(x, y, z) + yP_L(x, y, z) = 0$$

$$(2) P_K(x, y, z) = 1$$

when K is an unknotted circle. Relation (1) is inspired by a property of Alexander and Jones polynomials, and both of these can be expressed in terms of P . But the new invariant has stronger properties. For example, for a left-handed trefoil knot it is $x^{-2}z^2 - 2x^{-1}y - x^{-2}y^2$, whereas for a right-handed trefoil it is $y^2z^2 - 2xy^{-1} - x^2y^{-2}$. Hence, the trefoil and its mirror image are different. A reef knot and a granny knot also have different invariants P , and hence are inequivalent. Both of these are known results, but until now they have had very difficult proofs and cannot be obtained from the Alexander or Jones polynomials.

The proof of the existence of the invariant P is technical but relatively straightforward given the property of relation (1). It may be accomplished in several ways. Freyd and Yetter use a ring-theoretical argument involving braid groups. Hoste uses geometrical and combinatorial methods. Lickorish and Millett also use braids as well as some of Conway's ideas about tangles. Ocneanu's approach is similar to Jones's, involving number theory and functional analysis.

The hard part is to recognize the importance of relation (1) to begin with: the idea is almost too simple to be credible. The surprise is that it really does work, and beautifully. Some ideas can be discovered at almost any time, but lie fallow for years until the moment is ripe: this would appear to be an extreme case. And mathematicians can take heart from this discovery — not every new idea need be more complicated than old ones. $\square$

Ian Stewart is in the Mathematics Institute, University of Warwick, Coventry CV4 7AL, UK.

$$\text{Trefoil } P_L = yz^{-1} + x^{-1}y^2z^{-1} - x^{-1}z,$$

$$\text{Figure eight } P_L = x^{-2}z^2 - 2x^{-1}y - x^{-2}y^2,$$

$$\text{Unknotted loop } P_L = y^{-2}z^2 - 2xy^{-1} - x^{-2}y^2,$$

$$\text{Unknotted loop } P_L = x^{-1}y^{-1}z^2 - xy^{-1} - x^{-1}y - 1.$$

A question of new journals

One evening, at a quiet watering hole in Boston, or Oxford, three species meet who are rarely seen together, night or day — an academic (A), a librarian (L) and a publisher (P). Soon the talk turns from international politics to another matter of common interest . . .

A: . . . talking of non-proliferation, what we need is a non-proliferation treaty for journals.

L: Right! Our purchasing budget has just been cut in real terms for the tenth year in a row — it seems crazy to start yet more titles.

P: Another drink?

A: Scotch again, please . . . yes, there are already 15 possible journals for my next paper — that's more than enough.

L: Scotch for me too. . . . Do you know that now there's even an on-line database which deals specifically with new journal titles? It only covers the last three years or so but it's already got hundreds of entries.

At our library, we cut out multiple subscriptions to journals years ago; we started spending proportionately less on books than journals; then we started analysing usage patterns and suggested possibilities for other cuts.

A: I remember that at our campus — turned out that old Dr Croak had ordered five titles in 1958 (just after Sputnik) which no one else had ever heard of or used. Croak died in '62 and we were still taking them in '74.

L: Then we brought in the "you can only have a new one if you drop an old one" rule; now we've got everybody used to an annual round of cuts — last year we even had some money over after cutting too hard — a bit embarrassing.

P [to the barman]: Two Scotches and a tomato juice, please. . . . Of course, libraries have suffered to different degrees in different parts of the world. For librarians in Britain the strong dollar has meant a difficult time. But it has helped American libraries in buying foreign journals . . .

L: Except where foreign publishers price in dollars at enormous conversion rates.

P: I wouldn't condone that, but of course there are good reasons for some of the differentials, like airfreight and the higher cost of communication with subscribers, as well as a slight hedge against fluctuations in the exchange rate . . .

A: And I'm sure they're very interesting, but we're getting a little off the point. Now, is there a serious case to be made for new journals?

P: I think there is, but not for all new journals. And in many cases publishers would like nothing better than to be able to expand their largest journals while maintaining circulation, but it's usually not on.

There are a number of pressures on

publishers as well as libraries, and sometimes journals are started for reasons other than scientific need. But it's pretty difficult, in many cases, to sort out the mix of motives that go into the creation of a journal. I'm not going to defend all the proliferation, just because in some cases I think it's a good thing.

L: I'm not sure I follow you.

A: I'm not sure, either. I do know that probably 80 per cent of the research papers that are published are rubbish . . .

P: Well, what I mean is that there are some straightforward commercial reasons for starting new journals — a successful journal will have very healthy cash flow (especially compared with books), and provide security and continuity, since print runs can be accurately estimated.

Then there's competition which takes at least three forms: first, there's the chance that another publisher will start a journal either in the area you were considering, or in part of an area of one of your existing journals. If it does, then a hard-pressed library specializing in that area may drop the subscription to your journal and take a new one. So you'd better start it yourself.

And there's competition for authors — if a new specialist journal (or even a new journal in a new multidisciplinary area) starts up, authors might submit papers to it instead of yours — so again, a preemptive strike is called for. I'm sure there was a third type of competition . . .

A: Just what I thought — unnecessary proliferation of journals . . . [sotto voce] and of competition. . . . Of course, I know journals do compete, not usually overtly, for authors, but it's difficult and almost unpleasant to think of them competing for sales. Academic journals shouldn't be like washing powder — each title is unique.

L: From the leaflets and special offers I get from publishers, I'd say they're getting more like washing powder all the time.

P: Ironically, the mixture of fear and commercialism that I mentioned, and the resulting new titles, are partly caused by the library cuts that make it difficult for you to believe that it can make sense to start new journals. The long-term decline in the circulations of the established journals is also relevant. As that happened, some of the largest publishers decided to start new specialist journals which, they hoped, would bolster them if the decline continued.

L: Although that was likely to hasten the decline?

P: But you're forgetting the competition element — they may have had no choice, and they thought it was better that someone else suffered, not them. And then, of course, there was the extra fear that some of the decline was caused by library resource sharing, and the distribution of photocopies of journal articles by . . .

L: I was wondering when that would come up. I've seen figures on journal cancellation decisions and the reasons for them which show categorically that such decisions are totally unrelated to the availability of photocopies from . . .

P: But I don't wish to argue about that now . . .

A: Neither do I, now or any other time — let's have another drink. Same again? [L and P nod.]

P: I only mentioned it as another concern of publishers which, rightly or wrongly, was a spur towards the creation of new journals.

A: Well, if those are the pressures or motives, what's the serious case?

P: Perhaps I can work towards it. First, we have the view — some may call it simplistic — that a successful journal is its own justification. That is, the fact that authors submit papers and others buy the journal demonstrates the need. Unless authors are easily led by the glamour of a new publication in their specialty [L nods] or libraries are indiscriminating in their purchases [A nods] . . .

L: For the most part libraries still rely on the recommendation of their users before taking out a subscription.

P: And, for all the market research you may do there is no real quantitative measure of need other than the willingness of people to write, and other people to pay, as shown by trying to launch the journal. The risks, however, can be large — these figures [rummages in briefcase] will give you some idea. Let's assume this is for the first year of a brand new "commercial" journal (that's one with no direct involvement of a learned society) — starting small, say 80 pages an issue, and quarterly, with quite a lot of scientific notation and math. Here's the rough breakdown of costs:

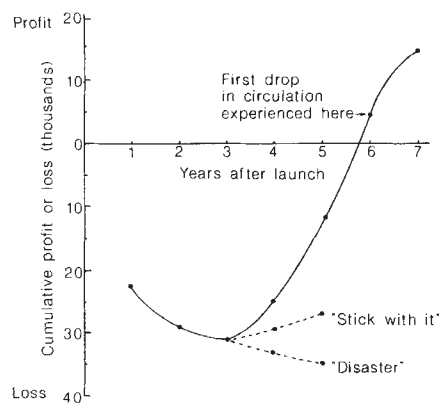
Typical small new journal costs in the first year

Typesetting	10,500
Printing and binding	3,800
Paper	2,000
Distribution	1,500
Editorial costs (copy editing and general overhead)	6,000
Honoraria	1,200
Marketing for first volume	10,000
Total	35,000

The marketing costs, of course, are high in the first year (they will be again in the third year, probably) and include such things as the production of extra copies of the journal to give away as promotion. So, in comparison with the cash flow

advantages of an established journal, there is quite a lot of "up front" investment.

Now, let's assume that the journal gets up to a circulation of 400 or 500 within four or five years, which wouldn't be untypical. The actual cumulative profit and loss will look something like this:



[Pointing] The dotted lines are for other, quite plausible scenarios. For example, the "stick with it" line is where the journal is running at a profit, but will take years and years to repay the initial investment. The "disaster" line is where the journal is running at a small loss each year, which means an awful lot of money down the drain in total.

A and L: And so the publisher shuts the journal down.

P: That does happen more often than it used to — but publishers will often try a number of things before giving up: changes of title and content, mergers, giving the journal to its editor . . .

L: But once that curve has gone up into the plus range, the publisher's laughing.

P: Well, it's worth a sigh of relief maybe. But the curve can go back down again.

A: All this doesn't explain how new journals can still do well despite the cuts in library funds.

P: We don't entirely understand it either. But there are several factors. In the early '70s many libraries switched funds from books to journals. They then cut multiple subscriptions, then poorly used titles and then foreign-language titles. This affected some publishers more than others — those who were starting new popular titles could gain at others' expense.

And in some fields there are a number of page-charge journals . . .

L: What exactly are they?

A: Humph . . . basically, where authors are asked to pay to get their work into print.

P: Oh we could be here until they throw us out debating that. The thing is that page charges cushion the publisher somewhat against circulation losses.

And there's another point. It's become a conventional wisdom that the individual subscriber to scholarly journals has almost disappeared, but in fact they have reappeared in a slightly different way — ironic really, since they are the members

of learned societies, the very species who were the first individual subscribers. In Western countries hundreds of learned societies have been formed in the past 20 years. Many of them have a journal, and many are published by various types of publisher. Often members receive reduced-rate copies, sometimes paid for in bulk by the society, which may then recoup the cost through general society membership subscriptions.

In effect, then, publishers have managed to tap a new source of revenue, which means that an even smaller number of sales to libraries can, overall, give a viable journal. On top of that, they've tried to control their own costs, to safeguard their margins while circulations have fallen. New technology at the publisher itself has had a limited effect so far, but changes in printing techniques and competition or recession in that industry have all helped.

Lastly, not all research areas, researchers or libraries are stuck for money, even now. If you can find the right topic, perhaps one where there is very heavy government and industrial investment, you might just get a winner, without managing to sell many to those libraries that are hard-pressed.

While we're on the subject, wasn't it you [to L] who was telling me last week about your new computerized circulation control system, your online connections to cataloguing systems and other databases, and your experiments on satellite transmission of journal articles, videodisks and CDROMs? Where does the money for all that come from?

L: Oh, that comes under a different budget allocation in our case — our paymasters still take a different attitude if we can show that we're into something sexy like new information technology. . . . My turn for drinks, I think. [Turning to the barman] Same again, please.

A: What's the rest of the justification for new journals?

P: Simply this. Scientific research is in a state of continual change. While the old basic disciplines remain, new research fields are always forming which may be more specialized, or involve new inter- or multidisciplinary links. To the extent that the scholarly journal is a vehicle for the communication of ideas, it makes sense for those new fields to have a specific journal as a forum rather than the ideas being spread across and possibly lost in the enormous quantity of scientific papers published in other specialized journals or large journals of broad and marginal relevance. Such specialized journals can be backed up by retrieval systems (abstracts journals, databases, librarians and so on) to enable the researchers to find papers from other journals on topics that intersect with their field.

You might ask: "Why not rely on the retrieval system from the start?" But no retrieval system is yet sufficiently good (or

sufficiently convenient) for any scientist to be well served by just a few enormous, monolithic journals which act as paper databases, backed up with, say, their machine readable counterparts . . .

L: What's that about "to the extent that journals are for communication"? . . . And I'm not sure I like being described as a retrieval system . . .

P: I just meant that journals have other functions too.

L: Oh, yes . . . brownie points, publish or perish and that sort of thing.

A: No, the process of publication is much more fundamental than that . . . it is an integral part of science. The submission of a paper before your peers; the recognition that the work is at least worthy of appearing (even if 80 per cent of it is rubbish); even the process of doing the refereeing are all parts of mature science.

L: Mmm, yes . . . brownie points. And if 80 per cent of it is rubbish, what does that say about scientific research — shouldn't we be worrying more about that than journal proliferation?

A: I think you misunderstand me . . .

P: There is also the view that there are now two types of journal — those for communication and those for archive, which is really only delayed or potential communication.

But to me the fundamental point is that a massive journal with, say, 3,000 circulation, doesn't necessarily serve the cause of science more efficiently or effectively than, say, eight more-specialized and more targeted smaller journals containing in total the same number of papers but with smaller overlapping circulations of 500 each. It's easier to make the opposite case since, for example, the single, large journal uses six times as much paper.

L: Does it? This is all getting rather academic . . .

P: In fact, there seems good reason to believe that the creation of new journals, whether out of old monolithic titles, or by focusing on a new field hitherto spread across a number of titles and disciplines, can lead to a system better able to respond to changes in research fronts. At least they provide the research worker with a core of work, most of which has a high degree of relevance.

A: Now that you mention it, my field is covered — I might have said — by at least 15 journals which all relate to it in some way. Perhaps it's about time there was just one place where these papers could be brought together . . .

P: That's interesting — are you free to discuss it over lunch next week?

L: [Expletive deleted] . . . someone, please, give me a drink. □

Alan Singleton, who eavesdropped on this conversation, is Research and Development Manager in the Publishing Division of the Institute of Physics and John Wright and Sons, Techno House, Redcliffe Way, Bristol BS1 6NX, UK.

New journals June 1983 to May 1984

CRITERIA for journals to be considered for review in this issue were circulated to publishers earlier this year, and were also published in *Nature*. They were that:

- (i) the first number appeared, or the journal was re-titled, between June 1983 and May 1984 (although journals not covered in last year's review issue were also considered);*
- (ii) the journal is published at least three times a year (one exception has been made to this rule);
- (iii) the main language used is English;
- (iv) where possible at least four issues should be made available for review, including the first and the most recent.

Last year's journals review supplement covered publications appearing between June 1982 and May 1983 and the second cut-off date, May 1984, allows for enough issues of a journal to have been published for a reasonable sample to be available for judgement (most are quarterlies). A spread of four different issues is taken as

* See *Nature* 311, 309–330 (1984). For previous journals review supplements see *Nature* 305, 477–497 (1983); 299, 491–514 (1982); and 293, 341–369 (1981).

the usual minimum on which reviewers' comments can be based.

Several journals known to satisfy the above criteria were not submitted for review, or arrived only in August or September, and therefore are not covered in this issue. It proved difficult to find reviewers for other, doubtless worthy journals, while some titles were considered to be of marginal interest to *Nature's* audience.

The brief given to reviewers was to limit themselves to comment on the publications sent to them, and to avoid discussion of general questions of periodical publishing. Opinions expressed in the reviews are based on a sample, and apply to mid-1984 at the latest. As in previous years, the preponderance of journals in the biological sciences reflects the bias of material submitted for review.

Details of editors and frequency of publication, and the subscription rates appearing at the top of each review, are given in most instances for 1986. This information is not complete in all cases, and readers interested in subscribing to a particular journal should check the rates with the publisher concerned. □

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• Among other titles submitted: *Annals of Sports Medicine* (Oxford University Press); *Blood Purification* (Karger); *C₁ Molecule Chemistry* (Harwood); *Earth, Moon, and Planets*, formerly *The Moon and the Planets* (Reidel); *Hazardous Waste* (Mary Ann Liebert); *Journal of Clinical Neurophysiology* (Raven); *Journal of Coastal Research* (The Coastal Education and Research Foundation, PO Box 2473, Fort Lauderdale, Florida 33303, USA); *Journal of Pineal Research* (Alan R. Liss); *Marine Resource Economics* (Crane Russak); *Medical Oncology and Tumor Pharmacotherapy* (Pergamon); *Microcirculation, Endothelium, and Lymphatics* (Deerfield Scientific Publishers); *Nuclear Engineering and Design/Fusion* (North-Holland); *Order: A Journal on the Theory of Ordered Sets and its Applications* (Reidel); *Remote Sensing Reviews* (Harwood).

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Journal of Experimental Pathology. Editor Robert M. Friedman.

Mary Ann Liebert. 4/yr. North America \$95, elsewhere \$123.

New immunology journals keep appearing with Malthusian enthusiasm. Some of them clearly fill a need in a still rapidly expanding scientific discipline; for others an early demise is devoutly to be wished. Take *AIDS Research*. Every major scientific and medical hebdomadal as well as a number of monthly journals have publicly



stated that they are giving top priority to reporting basic clinical advances in work on the disease. The appearance of this new journal has not so far materially aided the effort. A large part of *AIDS Research* has been devoted to hypothesis, guidelines, commentary and case reports. I have long ago taken against the camera-ready format and this addition to that travesty on the printer's art only reinforces my prejudices. AIDS is a vexing and frightening disease. A solution to the problems of prevention and therapy is urgently needed. Nothing could be more gratifying now than to superannuate this journal.

Not since the Lollards declined to participate in the performances of the Corpus Christi plays has any subject been scrutinized with more scholastic vigour than the complement system. Complement research has survived eight decades without a journal entitled *Complement* and the unheralded appearance at this late date of such a journal raises the spectre of this field's becoming decadent. Frankly, *Complement* is thin in original articles but so far rich in review articles, meeting reports and abstracts from meetings. It had unfortunate beginnings in a historical perspective on the subject by the late Manfred Mayer, that reminded me of the quip that a historian is one who predicts history. The genes of the complement proteins are now being cloned with great rapidity, giving rise to a great deal of excitement in the field, but so far *Complement* has not been

the vehicle for publishing this innovative stuff.

On the other hand, Springer-Verlag has brought forth a highly successful new journal, *JMCI: The Journal of Molecular and Cellular Immunology*. Richard Gershon, the founding editor, had the bright and invigorating idea of publishing reviewers' critiques and the authors' response at the end of each article. Interspersed among the original papers is lively invited commentary. Following Gershon's untimely death, almost coincident with the appearance of the first issue, Charles A. Janeway Jr has continued to steer this journal in the right direction. The content of *JMCI* is of high quality. Lag time from final submission to publication is minimal. The composition of the editorial board and editorial advisory board is outstanding. This journal should be added to every library that aspires to keep up to date with high-quality science.

There was a time when I thought I could define "immunogenetics". The word now

conjugates up confused images in my mind. Is it about immune response genes; or linkage markers of immunologically relevant proteins with diseases; or the molecular biology of immunoglobulin genes and T-cell receptor genes; or genetic polymorphisms of cell surface antigens detected with monoclonal antibodies; or all of these things? A large body of information is accumulating with the hori-



zons expanding faster than can be properly assimilated. Of the two new entries in this field, *Disease Markers* and *Experimental and Clinical Immunogenetics*, the former has a slight edge in the breadth and quality of its contents. Both, however, include good review articles and meeting reports, and the editorial boards have a very international flavour which is reflected in the broad geographical origin of the contributions. Both are published quarterly and appear to be good value.

I suppose one should be cheered by the emergence of a publication covering experimental pathology as a whole. In this time of increasing specialization and rising barriers between scientific disciplines, it is very courageous to start up such a journal. The prolixity of the contents of *Journal of Experimental Pathology* is so great as to flatter the appetite of dilettantes. Many good contributions appear in this new quarterly, and if it survives the temper of these times I will be gratified — but surprised. □

Fred S. Rosen is the James L. Gamble Professor of Pediatrics, Harvard Medical School, Immunology Division, Children's Hospital Medical Center, 300 Longwood Avenue, Boston, MA 02115, USA.

Up with the trends

Robert Freedman

BioEssays: News and Reviews in Molecular, Cellular and Developmental Biology.

Editor-in-chief W.J. Whelan. Cambridge University Press. 12/yr in two volumes. UK £34 (institutional), £15 (individual); North America \$70 (institutional), \$24.50 (individual).

BioEssays is the offspring of the ICSU (International Council of Scientific Unions), just as *TIBS* (*Trends in Biochemical Sciences*), the first of the successful *Trends* journals, was the offspring of the International Union of Biochemistry. This is stated explicitly in the opening editorials of the first issue, where it is also acknowledged that ICSU has made this entry into publishing in order to increase its visibility, its influence — and its income.

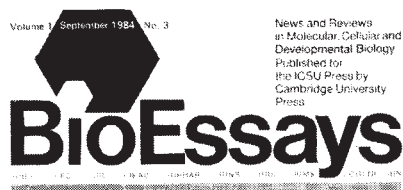
Comparison with the *Trends* series is unavoidable; the journals are even published in the same city (Cambridge, England) though by different presses, and the founding editor-in-chief of *BioEssays*, (W.J. Whelan) was the first editor-in-chief of *TIBS*. So it is no surprise that in format and flavour *BioEssays* is familiar. The journal is an unglossy monthly, of about 50 pages per issue, each containing six short reviews (four to five A4 pages), plus features, comment, historical notes and book reviews.

The crucially individual aspect of *BioEssays* is indicated on the front cover by a series of inscrutable acronyms (IUBS, IUPS, IUPHAR, IUNS, IUIS . . .) which refer to the nine distinct international scientific unions which are promoting the journal. Between them these organizations represent the whole range of the biological sciences, and the journal's sponsors have clearly intended it to tap the growing body of work in which

modern molecular and cell biology are applied to a variety of traditional biological questions. The journal's subtitle, *News and Reviews in Molecular, Cellular and Developmental Biology*, covers an enormous and growing field, but one which does not belong wholly inside any of the current *Trends* journals nor wholly inside any national scientific societies or international unions.

Does the existence and growth of work crossing the boundaries of the current mainstream disciplines warrant a distinct new review journal? Many articles in *BioEssays* would fit comfortably into *Trends in Biochemistry*, *Trends in Genetics* or *Immunology Today*. But on the evidence of the 12 issues available for review it appears that *BioEssays*, though broad in scope, is essentially filling the niche caused by the absence of a *Trends in Cell Biology*, and by the enforced brevity of the mini-reviews in *Cell*.

Seen in those terms, there is no doubt



that the journal meets a genuine need and meets it well. The reviews are authoritative and clear, the occasional other articles are lively and the journal is generally well-written. It is not faultless, however. I find it rather dull to look at; even the best micrographs seem to lose impact on the fussy front cover, and some of the cover diagrams have been dismal. And it seems to me that the well-trying mixture of news and reviews is executed here without any striking originality. Still, this formula is well-trying, precisely because it works. The short review gives enough scope for the author to convey results, opinions, arguments and sources, while not burdening the reader with too much detail. The features — articles on key laboratories, historical pieces, social comment, meeting reports — provide variety and frequently offer the seductive combination of enlightenment and gossip.

There is even a straightfaced regular column entitled "The Airport Professor" which purports, with great seriousness, to give advice on the best currency in which to buy air tickets, the best seats to ask for in a 747, warnings on dubious credit cards, advice on hire car rates, notes on road works near Singapore Airport, and so on. With a few pearls from "The Airport Professor" — did you know that departure tax at Mexico City Airport can be paid only in local currency? — no one need confess to a summer confined to the laboratory and the camp-site. □

Robert Freedman is Senior Lecturer in the Biological Laboratory, University of Kent, Canterbury, Kent CT2 7NJ, UK.

Looking at protocol

Kim Kaiser

Gene Analysis Techniques. Editors Jack G. Chirikjian and Takis S. Papas. Elsevier, New York. 6/yr. North America \$68 (institutional), \$34 (individual); elsewhere \$85 (institutional), \$51 (individual).

New techniques arrive so thick and fast in molecular biology that I for one find it difficult to keep up with them, especially as they are often hidden away in the materials and methods sections of papers I have no other interest in. Moreover, as I suspect do most other people, I tend to resist changing from a familiar method until either a new technique has proved so popular with my colleagues that it is difficult to ignore it, or it has become codified in such experimental manuals as those published by Cold Spring Harbor Laboratory. Unfortunately (but inevitably) these manuals are to some extent out of date at the time of publication, yet they are still treated as bibles several years later.

In a way this is not a bad thing. That a procedure works is of prime importance and news of anything radically different quickly works its way through the grapevine. On the other hand, more-or-less minor improvements that make a technique simpler, cheaper or more efficient are discovered from time to time, and it would be useful to have a forum whereby such improvements can be brought quickly to the attention of the laboratory worker. That such a need exists is exemplified by the success of newsletters such as Bethesda Research Laboratory's *Focus*. *Focus* articles are not refereed but feedback is accepted from readers.

Roughly half of the contributions to *Gene Analysis Techniques*, which still contains only three articles per issue halfway into its second year of publication, are relatively simple modifications of or comments upon existing experimental protocols. Into this category fall papers such as that describing the successful substitu-



Gene Analysis Techniques

tion of cheap non-fat dried milk for the "Denhardt's ingredients" and sheared DNA of a hybridization mixture, one describing parameters that greatly enhance the efficiency of oligonucleotide extension during mutagenesis of DNA fragments in M13 vectors, and attempts to quantitate the efficiency with which genes introduced into mammalian cells are expressed. The rest of the papers concern newly developed techniques. Into this category fall both genuinely useful papers (many of

which are of limited general interest, however), as well as some describing no doubt worthy techniques that are unlikely to be taken up by anybody but the inventor's colleagues since alternative and sometimes simpler methods are already in common use.

The production standard of the journal is good, papers appear at most four to five months after being received, and no doubt the cost of subscription would be saved if even a few of us substituted dried milk for BSA and salmon sperm DNA. However, no individual is likely to be interested in any but a proportion of the limited number of contributions each year. If the journal were available in our central university library I would make an effort to look at back issues once or twice a year as, I am sure, would many of my colleagues. It is too expensive, however, for our departmental library and not worth a personal subscription. Lastly, I would suggest to the editors that they provide a forum for discussion or updating of the published material. □

Kim Kaiser is a Lecturer in the Department of Genetics, University of Glasgow, Church Street, Glasgow G11 5JS, UK.

Ideas of oncology

John M. Goldman

Critical Reviews in Oncology/Hematology. Editor Stephen Davis. CRC Press. 4/yr. North America \$104, elsewhere \$124.

Hematological Oncology. Editors J. W. Parker, R.J. Lukes, G.P. Canellos and J.M.A. Whitehouse. Wiley 4/yr. UK £62 (institutional), £46.50 (individual), £31 (student); North America \$120 (institutional), \$90 (individual), \$60 (student).

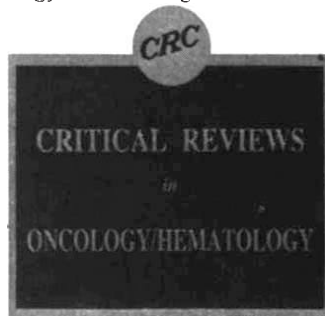
THE AIM of *Critical Reviews in Oncology/Hematology* is "to compile manuscripts . . . which summarize evolving concepts within the broad disciplines of oncology and hematology . . . [The] subject matter will be discussed in a timely, critical and analytical manner".

In practice the journal follows the standard CRC *Critical Reviews* format. The editor invites two or three reviews on widely differing topics for each issue, and then submits the finished manuscript to an independent referee whose job is to correct errors and draw attention to omissions. The result in most cases is an excellent and comprehensive review, such as "Staging for conservative management of Hodgkin's disease", "Monoclonal antibodies in cancer", "The fibrinolytic system in man" or "Internal mammary scintigraphy", written by undoubted experts in the field. Each review runs to about 25 or 30 pages. The number of references varies from about 100 to more than 500.

I can see just two drawbacks in this approach. First, the very wide range of

subjects which the editor attempts to cover, and the fact that so few reviews actually appear in each number, mean that the specialist reader will be lucky to find even one article of specific interest in a year's issues. Secondly, the way in which the issues are produced suggests that the interval between the submission of a manuscript and its eventual appearance in print may be quite substantial, perhaps more than a year. For some subjects this may not matter too much — I was fascinated to read that early allusions to fibrinolysis can be found in the work of Hippocrates — but in other, fast-moving areas such delays can be frustrating. These reservations notwithstanding, the scientific standard is undoubtedly high and all medical libraries will need to subscribe.

The scope of *Hematological Oncology*, defined in the editorial in the first issue, is also wide, not to say formidable — "pathology, radiodiagnosis, radiation



therapy, medical oncology, immunology, virology, epidemiology, tissue culture, *in vitro* drug testing, cytogenetics, cell kinetics, receptor assays, HLA studies and other related areas", to mention only some of the topics. This must mean that the journal will consider virtually any contribution in the field of oncology, though in practice the contents reflect the editors' particular interests (the immunopathology, clinical features and treatment of lymphoproliferative disorders). Papers on cell lines, cytogenetics and oncogenic viruses are also well represented.

The bulk of each issue consists of original research papers of somewhat variable quality, but the editors have solicited and published a number of valuable review articles — on simian AIDS, the Kiel classification of non-Hodgkin's lymphoma and purging bone marrow before autografting, for example. Also included are short communications, book reviews and a forum in which individual topics are addressed by chosen authors; letters from readers are invited. It appears that the time from acceptance to publication is agreeably short.

Overall, this journal looks like being a useful addition to the oncological literature. But perhaps its precise content needs to be somewhat more narrowly defined for the future. □

John M. Goldman is in the Medical Research Council's Leukaemia Unit at the Royal Postgraduate Medical School, Hammersmith Hospital, Ducane Road, London W12 0HS, UK.

Cosmopolitan agents in context

B. L. Ginsborg

Biogenic Amines: The International Interdisciplinary Journal Reporting Basic and Clinical Research on Biogenic Amines and Aminoacid Transmitters. Chief editors H. Parvez and T. Nagatsu. VNU Science Press. 6/yr. Surface DM 378, air DM 390.

Biogenic Amines is published in Utrecht; its price is set in deutschmark; its editors-in-chief are Parvez from Paris and Nagatsu from Nagoya; and its editorial board of some 50 members is drawn from eleven different countries, and includes Axelrod from Bethesda, Sandler from London, Lapin from Leningrad and Seeman from Toronto. In a sample of four issues, amounting to about 320 pages, thirteen articles are from Japan, five from the GDR and the remaining fifteen from eleven other countries.

Among the titles of papers in the sample are "Oxidation of acetylpolymamines by amine oxidases from soybean and oat seedlings", "A sensitive assay for β -phenylethylamine in biological samples by gas chromatography/chemical ionization mass spectrometry", "Tyramine-induced suppression of central noradrenergic neurons following monoamine oxidase inhibition" and "Elevated levels of polymamines and radioimmunoassayable 6-hydroxymethylpterin-like compound in urine from cancer patients". The dominant subject of investigation is the rat (seventeen articles) but also studied are man (five articles), the goat, chicken, dog, goldfish, rabbit and bovine adrenal medulla. From all this it is evident that the publisher's description of the journal as "international and interdisciplinary . . . reporting basic and clinical research" would not contravene any trade-description act.

The papers are in English, and have the standard format of introduction, methods, results, discussion and refer-



ences. There are no page charges. Clearly, *Biogenic Amines* could provide an alternative home for papers which might otherwise have appeared, at least in respect of their subject matter, in established journals of biochemistry, pharmacology, analytical methods or neuroscience. But my guess is that authors will generally continue to send their more exciting work to a journal of the appropriate discipline.

It is true that there are successful journals concerned exclusively with particular

classes of agents of biological interest, such as cyclic nucleotides, neuropeptides and prostaglandins to mention but three. However these are substances in their adolescence which attract enthusiastic, single-minded followers determined to assign to them as many biological functions as possible. By contrast, amines already occupy positions of undisputed importance in the biological scheme of things. They do not seem to me to require positive discrimination in the form of an exclusive publication. □

B. L. Ginsborg is a Professor in the Department of Pharmacology, University of Edinburgh, 1 George Square, Edinburgh, EH8 9JZ, UK.

Periodical changes

A. J. Leigh Brown

Molecular Biology and Evolution. Editor-in-chief Walter M. Fitch. University of Chicago Press. 6/yr. North America \$60 (institutional), \$30 (individual); elsewhere \$64 (institutional), \$34 (individual).

IN RECENT years, the molecular approach to evolutionary biology has proved very fruitful. Few would dispute the interest engendered by the mass of data coming from this source, although it may be some time before our understanding of the process of adaptive evolution is greatly advanced by them. In these circumstances it is hardly surprising that a new journal should appear, although the impetus for the appearance of *Molecular Biology and Evolution* came from scientists, rather than a publishing company. Perhaps in consequence, the subscription price is very reasonable, but it remains to be seen whether the journal will fulfil all the hopes of its editors.

One of the intentions of the journal is to bring together articles covering the broad field of molecular aspects of evolution. Certainly, the contributions published to date might previously have appeared in a very wide range of journals so this aim has been fulfilled. They present evolutionary studies which utilize nucleic acid sequences, restriction maps, immunological distances and enzyme polymorphism, and both prokaryotic and eukaryotic systems are well represented. There are regular theoretical contributions also; these are closely related to experimental work and fit in well with the overall theme. Papers of all lengths have been published, and a few reviews, book reviews and an occasional letter to the editor have also appeared. The quality of many of the articles has been very high.

Each number of *Molecular Biology and Evolution* contains five or six papers. Surprisingly, the journal has not expanded since its first issues and perhaps it has not yet caught the attention of molecular biologists *en masse*. Some features may be

acting as a deterrent. Evolutionary biologists have a relatively leisurely life when it comes to reading the current literature, with a handful of relevant journals producing perhaps 50–60 papers a month in all, but molecular biologists might be

Molecular Biology and Evolution

faced with five times as many. A new publication will clearly have to offer something extra to attract the attention of the beleaguered molecular biologist. Some pointers can be found among the more successful journals covering the subject — large formats, which allow bigger, better produced figures and tables; distinguishing the results from the materials and methods section by position or typeface; and, finally, quick publication.

Molecular Biology and Evolution falls down in these respects. Some of the illustrations have been quite clear, but others have been cramped, and some DNA sequences have been very poorly reproduced. The small page size and lack of distinction between sections makes it difficult to jump to the key results of a piece of work. And six months, which seems to be the norm, is now a long time between acceptance and publication. While the subscription price is much more attractive, these adverse points will not have helped the journal to establish itself alongside the *Journal of Molecular Evolution*. □

Andrew Leigh Brown is a Lecturer in the Department of Genetics, University of Edinburgh, King's Buildings, West Mains Road, Edinburgh EH9 3JN, UK.

Heredity in disorder

D. F. Roberts

Genetic Epidemiology. Editor-in-chief D. C. Rao. *Alan R. Liss*. 4/yr. North America \$190 (institutional), \$90 (individual); elsewhere \$213 (institutional), \$113 (individual).

THE first reference to epidemiology in the genetic context seems to have been in *Human Heredity* (1954), where Neel and Schull pointed out its value in helping clarify the contributions of heredity and environment to the aetiology of a disorder. This is one of the reasons given for the launch of *Genetic Epidemiology*, a term more frequently used in North America than in Europe. Other reasons are to help in the interpretation of our increasing knowledge of DNA structure, and in understanding the genetic effects of the introduction into the environment of potentially mutagenic agents.

An appreciable proportion of the papers in the four issues of Vol. 1 are in the

first category, for example that on the measurement of the genetic contribution to breast cancer in Denmark, but only one deals with a DNA probe and none relates specifically to mutational effects. The general content is wider. Some papers, for example one on coeliac disease, are based on heterogeneous samples from several populations, are concerned exclusively with genetic analysis and have little epidemiological content. There are several, too, that are theoretical in nature, concerned with techniques rather than their application, and have little claim to be of particular relevance to genetic epidemiology.

These articles — indeed all of the contributions in the first volume — would not have been out of place in many of the established journals on human genetics. Why then introduce a new one? Neel (p. 6) points out that *Genetic Epidemiology* will provide a common forum for all those whose various interests impinge on the subject. But Motulsky (p. 144) sounds a word of caution: this new journal should not result in the erection of barriers

GENETIC EPIDEMIOLOGY

around a small group of researchers who use complex methods which they alone understand, and who do not communicate with biological and medical workers.

The papers are of varying lengths, but of a uniformly high standard. Despite the rigorous refereeing procedure, Vol. 1 (published in 1984) includes articles accepted up to September of that year, so obviously processing of manuscripts is prompt. The quality of production is rather better than some of the other Alan Liss titles, but the journal is not particularly cheap.

Genetic Epidemiology will perform a valuable function if it concentrates on material that is strictly concerned with the subject implied by its title. If it is broader in scope, as the first volume is, it may also be useful in relieving the pressure on established journals. Certainly, given the quality of the articles published to date, it deserves to succeed. □

D. F. Roberts is Professor in the Department of Human Genetics, University of Newcastle upon Tyne, 19 Claremont Place, Newcastle upon Tyne, NE2 4AA, UK.

Autumn books

Nature's next review supplement is Autumn books, which appears on 14 November. Among the books to be reviewed are *Vaulting Ambition* (by Philip Kitcher); *The Joy of Science* (by Carl J. Sindermann); *Einstein in America* (by Jamie Sayen); *The Dialectical Biologist* (by Richard Levins and Richard Lewontin); *Seven Clues to the Origin of Life* (by A.G. Cairns-Smith); *Superpower Games* (by Steven J. Brams); and *The World Food Problem 1950 – 1980* (by David Grigg).

Into ultrastructure

Audrey Glauert

Journal of Electron Microscopy Technique. Editor-in-chief John E. Johnson, Jr. *Alan R. Liss*. 8/yr. North America \$175 (institutional), \$85 (individual); elsewhere \$199 (institutional), \$109 (individual).

ELECTRON microscopy is flourishing and continues to make major contributions to our understanding of the ultrastructure of materials of diverse origin, from moon dust to the biological macromolecules which are fundamental to living processes. A basic core of techniques is now well established but there has never ceased to be expansion in the scope of electron microscopy, resulting from the development of new instruments and advances in their mode of operation, and from the increasing sophistication of methods for image analysis and for preparing specimens for examination.

In this sense, electron microscopy is still a young science with a consequent need of a vigorous journal literature to disseminate technical information quickly and as widely as possible. This task is ably performed by established publications (such as the *Journal of Microscopy*, *Micron* and *Microscopica Acta* and *Ultramicroscopy*) and so there arises the inevitable question — why yet another journal?

As its title declares, the aim of the *Journal of Electron Microscopy Technique* is to publish detailed articles on methods in electron microscopy. The danger for such a journal is that it may become an outlet for second-rate papers describing results with little methodology, and it is gratifying to see that this new publication has admirably followed its own guidelines so far. In this, however, it does not differ from existing journals. In particular it has much in common with the *Journal of Microscopy*, on which it appears to be modelled (a compliment for the latter; imitation is the sincerest form of flattery).

There will inevitably be some competition between the two journals but this may be no bad thing. The *Journal of Microscopy* is unique in that it gives equal weight to all forms of microscopy, so that it plays a leading role in those fruitful areas where light and electron microscopy meet. It attracts contributions from a wide range of countries, especially in Europe, while the *Journal of Electron Microscopy Technique* has already shown itself to be popular in North America. There are always advantages in publishing nearer home. If the *Journal of Electron Microscopy Technique* can maintain the high standards of these early issues it deserves to succeed. □

Audrey Glauert is at the Strangeways Research Laboratory, Worts' Causeway, Cambridge CB1 4RN, UK. She is editor of the series *Practical Methods in Electron Microscopy*, published by Elsevier.

Viruses in medicine and in science

D.J. Rowlands

Vaccine. Editor R.E. Spier. *Butterworths*. 4/yr. UK £82 (institutional), £20 (individual); North America \$162 (institutional), \$40 (individual).

Virus Research: An International Journal of Molecular and Cellular Virology. Editors-in-chief Brian Mahy and Richard Compans. *Elsevier*. 8/yr. Dfl. 448, \$154.48.

ADVANCES of the past few years, particularly in molecular biology and genetic engineering, have paved the way to novel approaches to vaccine technology which hitherto had basically remained unaltered since the days of Pasteur. So it is a propitious time to launch a new journal covering the wide range of topics relating to immunoprophylaxis, and *Vaccine* has set itself this task.

Many of the developments which may have great significance in future vaccine production are in areas at the forefront of molecular biology and immunology research, and consequently tend to appear in established "prestige" publications. *Vaccine*, however, is a very rounded journal in that it regularly includes editorial comment and readers' letters. Each issue also features a short review article on a topical subject, patent reports and a meetings' calendar. The editors have therefore produced a journal in the broadest sense as opposed to a collection of papers. The four issues comprising each volume include some 30 or so refereed original papers, published eight to nine months after submission. Most of the contributions are



concerned with virus vaccines and are submitted from many countries throughout the world. The price is reasonable.

Virus Research is a more specialized journal and does not have the interdisciplinary goals of *Vaccine*. Its scope is principally molecular aspects of virology, and it can therefore be seen as a rival to the long-established *Journal of Virology* and to a certain extent *Virology*. It is questionable whether a new journal was required in this particular arena but one or two features of the organization of *Virus Research* should give it some competitive advantages. Paramount amongst these is the arrangement of having a chief editor in both the United States and Britain, which should overcome the suspicion (whether well founded or not) of discrimination that some authors from Europe feel about submitting their work to American journals

and vice versa. Examination of several issues shows that authors from Europe and the United States are contributing similar numbers of papers, although it is probably too early in the journal's history for a stable pattern to have emerged. In contrast to *Journal of Virology*, *Virus Research* does not demand page charges, a great advantage at a time when research funding is lean.

The eight annual issues together contain some 50–60 papers, and these are refereed and appear about six months after submission. The quality of work published and the calibre of the authors is generally good. The overall standard of printing and presentation is quite acceptable (with the minor criticism that the paper used is of a type that allows printing on the reverse side of the page to show through to some extent, a point that also applies to *Vaccine*), and the price is not exorbitant.

A few meetings announcements apart, *Virus Research* contains no material ancillary to research papers. While it is stated that invited reviews will be published, none have appeared to date, and there is no space devoted to comment, either editorial or from readers. The journal is therefore a compendium of papers and

VIRUS RESEARCH

lacks the sense of involvement in its subject that is evident in *Vaccine*. It does, however, have its strengths, and it will be interesting to follow the evolution of this journal with respect to its major competitors in the United States. □

D.J. Rowlands is at Wellcome Biotechnology Limited, Ash Road, Pirbright, Woking, Surrey GU24 0NQ, UK.

The rivals in review

John Birch

Biotechnology Advances: Research Reviews and Patent Abstracts. Editors M. Moo-Young, J.D. Bu'lock, C.L. Cooney and B.R. Glick. *Pergamon*. 2/yr. UK £65 (institutional), £29 (individual); North America \$110 (institutional), \$50 (individual).

Critical Reviews in Biotechnology. Editors George G. Stewart and Inge Russell. *CRC Press*. 4/yr. North America \$104; elsewhere \$124.

PUBLISHING in biotechnology has been a growth industry over the past few years and it must be increasingly difficult to find a niche that is not already well served by an existing journal. This must be particularly true for these two journals, both of which were launched in 1983 as vehicles for review articles.

Pergamon's *Biotechnology Advances* has an unusual format, being made up principally of mini-reviews and patent abstracts with a very short section giving summaries of technical reports released, for example, by government agencies. The reviews are intended to address all the main areas of biotechnology, and indeed in the issues to date they have covered a wide range of topics, from recombinant DNA and monoclonal antibodies to waste-water treatment.

The editors have the declared aim of satisfying both the specialist and the generalist but in so doing may end up pleasing neither. Although the papers give extensive literature references, they are brief to the point of austerity and lack adequate discussion. Hence, while the specialist may find them rather superficial the generalist will find them very dry reading. One is further deterred from browsing through the journal by the unattractive

camera-ready script. This may be essential for rapid-publication journals but I really wonder whether it is necessary for a twice-yearly publication.

I did not find the patent abstract section particularly useful. It only covers US patents, is not as well done as in specialist publications such as *Derwent Biotechnology Abstracts* and, for commercial users at least, is infrequent. The abstracts are divided into subject areas on what seems at times to be a fairly arbitrary basis. This, combined with the absence of an index or any cross-references, makes the section awkward to use. The final part of the journal summarizing technical reports is again very brief and, as with the patents, there are better ways of accessing this information.

The CRC offering is an addition to their extensive list of *Critical Reviews* journals. To date at least it has concentrated on the applied process end of biotechnology, with articles on industrial enzymes, biomass and ethanol production as well as aspects of fermentation technology such as the use of immobilized cells. The journal is attractively produced and the reviews are well written. Topics are covered in considerable depth with typically two or three reviews per issue. Unusually, the paper's referees are cited.

The question with this journal, as with *Biotechnology Advances*, is whether it really fills a gap — there are already first-rate review publications in this area, such as *Advances in Biotechnological Processes* and *Advances in Biochemical Engineering/Biotechnology*. *Critical Reviews in Biotechnology* may find devotees in the particular areas they are addressing, but *Biotechnology Advances* could find it harder to achieve popularity with the general readership at which it is aimed. □

John Birch is Director of Fermentation and Downstream Processing at Celltech Limited, 244–250 Bath Road, Slough SL1 4DY, Berkshire, UK.

Talking of molecular stereodynamics

Struther Arnott

Journal of Biomolecular Structure & Dynamics. Editor-in-chief Ramaswamy H. Sarma. *Adenine Press, PO Box 355, Guilderland, New York 12084, USA.* 6/yr. \$351 (corporate), \$240 (institutional), \$99 (individual), \$60 (student).

SOME think that the State University of New York at Albany is an academic backwater, another memorial in elegant concrete to the brave but abortive efforts of the late Governor Rockefeller to mimic in his state the economic magnetism of the University of California system. Yet Albany has become magnetic in an unexpected way as a Mecca for the legions of (mainly nucleic acid) physical biochemists who are the intellectual offspring or grandchildren of the philoprogenitive pioneers of what passed for molecular biology in the 1950s and early 1960s. There is now a biennial pilgrimage to the "Conversations in Biomolecular Stereodynamics", whose efficient and verveful impresario is Ramaswamy Sarma.

As is now too often the case, these Conversations begat published proceedings. Then, to the surprise of many contributors but the dismay of only a few, the proceedings of the Third Conversation were transmuted into the first four or five numbers of the *Journal of Biomolecular Structure & Dynamics*.

Anyone who has had to swallow the sour draught of the patronizing reports

Journal of Biomolecular Structure & Dynamics

from the *Journal of Molecular Biology* must welcome a new journal which not only permits you to nominate your own referees, but urges you to list scientists who should not be allowed to referee your paper. The price of such a liberal policy is all too evident: poor articles with the spurious authority of plenty of numbers and good graphics have come to rest here after unsuccessful attempts to dock in more discriminating journals; strident articles that are more offensively partisan than is common; and potentially good articles that have been permitted to be self-indulgently prolix. Some editors have exploited this licence no less than their other authors. But reforms may be imminent. As a start, we are told, the editor responsible for accepting a paper will in future be advertised.

The production of the journal is "high tech". Potential authors are invited to submit manuscripts on computer tapes or floppy discs or by electronic transmission. Laser optics are used to read ordinary manuscripts and to set type. In-house copy editing has been profitably aban-

doned, and fastidiousness about English usage has been gaily abandoned. Nevertheless, successive numbers have been pleasant to read and look at, with ungrudging space for illustrations.

The popularity of the Conversations in Albany indicates that there is a gap for this journal to exploit. This interstitial niche is occupied by physical scientists on the fringes of biology who are concerned mainly with molecular structures. They have at their disposal increasingly powerful probes, such as nuclear magnetic resonance and X-ray diffraction, and tools such as computer graphics and even supercomputers. The preferred audience for their voluminous output is people like themselves, despite the obvious danger of intellectual incest through protection

from the proper darwinian pressures both from specialists in the technologies being used and from the biologists who should be defining the goals of this large investment in people and hardware.

Ironically the long-term scientific success of the *Journal of Biomolecular Structure & Dynamics* may be ensured only by divergent evolution from the phenotype that ensured its successful birth. That this may be possible is demonstrated by a recent policy decision to de-parochialize the board of editors, currently dominated by nucleic acid interests. Such a step is necessary. I doubt if it will prove sufficient. □

Struther Arnott is Vice President for Research and Dean of the Graduate School, Purdue University, West Lafayette, Indiana 47907, USA.

Resonating promise

David Gadian

Magnetic Resonance in Medicine. Editor-in-chief E. Raymond Andrew. *Academic.* 6/yr. UK £68.50, North America \$85 (for 1985).

Magnetic Resonance Imaging: An International Journal of Basic Research and Clinical Applications. Editors-in-chief John C. Gore and Francis W. Smith. *Pergamon.* 6/yr. UK £88 (institutional), £29 (individual); North America \$150 (institutional), \$50 (individual).

NUCLEAR magnetic resonance (NMR) is attracting considerable interest as a non-invasive method of obtaining images of the human body and of studying tissue metabolism. The related technique of electron paramagnetic resonance is also becoming increasingly used in biomedical research. Much of the work in this area is highly interdisciplinary, and established meetings and journals do not necessarily provide an appropriate forum for discussion or publication of research results; hence the emergence of two new societies and their associated journals.

Magnetic Resonance in Medicine, which is the official journal of the Society of Magnetic Resonance in Medicine, has taken the eminently sensible approach of adopting a similar format to the well-respected and well-established *Journal of Magnetic Resonance*. The journal includes regular papers, together with shorter communications and notes, and many of the recent papers have appeared within eight to nine months of submission. As the official journal of a flourishing society, the journal should be assured of a fairly wide readership, and it should attract contributions from the many magnetic resonance specialists who are now involved in biomedical research.

Magnetic Resonance Imaging is also the official publication of a new society, the Society of Magnetic Resonance Imaging.

Its emphasis differs somewhat from that of *Magnetic Resonance in Medicine*, in that rather more of the articles are clinically orientated, with many contributions coming from hospital research groups. Thus, as well as original scientific papers on physics, biology and medicine, clinical case reports are also published. In addition, an abstract service, book reviews, review articles and some invited articles are regular features. From time to time, the intention is to devote special numbers to areas of particular importance; for example a recent issue is concerned specifically with the use of contrast agents in magnetic resonance imaging.

In the short term, the success of these journals will depend on the number of high-quality papers that they attract, and in this respect they have taken steps in the right direction, with good editorial control and improving speed of publication. Further evidence of health is that both have progressed from quarterly to bimonthly publication. It might seem that the appearance of two new journals de-

Magnetic Resonance in Medicine

voted to this fairly specialized area is excessive. However, they do differ in their emphasis and approach, and if this distinction between them develops further then each should find its own niche. With regard to their long term prospects, magnetic resonance continues to advance in leaps and bounds forty years after the first successful NMR studies were performed, and there is every reason to believe that further developments will continue to justify the existence of these journals. □

David Gadian is Director of Physics in Relation to Surgery at the Royal College of Surgeons of England, 35-43 Lincoln's Inn Fields, London WC2A 3PN, UK.

Definition by doing

Andrew Miller

European Biophysics Journal. Managing editor Peter Bayley. Springer-Verlag. 6/yr. DM472, \$172.

WHAT is biophysics? Simply what biophysicists do? Better, it might seem, is a definition that emphasizes that biophysics is a technique-orientated subject: "the application of the concepts and methods of physics to problems in biology", perhaps.

If we take this response and compare it with what goes on in university departments of biophysics, or with the contents of biophysics journals, complications become evident. While most biophysicists specialize either in the determination of the molecular structure of biological macromolecules or in neurophysiology, the definition encompasses a much wider field including animal mechanics, environmental biophysics, transducer and radiation physics, and the application of microelectronics to biology. Research on topics such as these is usually carried out in more traditional departments — of physics, zoology or engineering, for example — not in departments of biophysics. Nor indeed is it dealt with in the *European Biophysics Journal*, the successor to *Biophysics of Structure and Mechanism*. Titles of the articles in the four issues available for review show an emphasis on biological membrane processes and on the application to biology of specific physical techniques, particularly nuclear magnetic resonance and photon correlation spectroscopy. Occasional theoretical articles also appear.

It may be that four issues is too small a sample from which to make a judgement, but it is surprising to find no papers on X-ray analyses. It is this physical approach that has had the greatest impact on biological science, and indeed it has led to the recognition of structural molecular biology — a problem-orientated rather than a technique-orientated discipline. Perhaps the researchers involved in this area of work tend to send their papers to other journals.

The editors state that the scope of their journal encompasses molecular structure and interactions, membrane and receptor biophysics, thermodynamics and energetics, and theoretical biophysics. This a fair description, with the proviso that molecular structure is rather weakly represented, and within this compass the papers are of good quality and of considerable interest. It also suggests that a nominalist attitude is appropriate and that biophysics is what biophysicists do. □

Andrew Miller is Professor in the Department of Biochemistry, University of Edinburgh Medical School, Hugh Robson Building, George Square, Edinburgh EH8 9XD.

Inside insects from North America

J. F. V. Vincent

Archives of Insect Biochemistry and Physiology. Executive editor Richard T. Mayer. Alan R. Liss. 6/yr. North America \$250 (institutional), \$85 (individual); elsewhere \$273 (institutional), \$108 (individual).

THIS is a journal which starts out with high standards — prospective authors are informed, in a remarkably complete "guide", that "Articles that are confirmatory in nature or deal with analytical methods previously described will not be accepted". To this list can be added reviews, book reviews, comment and reply.

Archives of Insect Biochemistry and Physiology, then, is solely a vehicle for original research papers. Acceptable areas are endocrinology, development, neurobiology, behaviour, pharmacology, nutrition, carbohydrates, lipids, enzymes, proteins, peptides, nucleic acids, molecular biology and toxicology. Clearly the emphasis is more on the biochemistry than the physiology of insects. The papers published to date have been a mixed bunch — some very good, a few rather poor (could these be the "invited" contributions so necessary in a new journal?) — and they vary in length from only 1,000 words to 4,000 or more. Each issue contains eight to ten papers.

Editorial style is mostly good, with tables, figures, summary and acknowledgements clearly set out. Not so the

references which are arranged in order of appearance in the text, a perverse system which reduces the usefulness of this essential part of any paper. The quality of production is really excellent, with very clear typefaces on glossy paper which takes half-tones very well, and the overall format is generous even though the subscription price is not high. Publication time is slow, however — an average of two months for refereeing and a further ten months before appearance.

Archives . . . is superficially in direct competition with Pergamon's *Journal of Insect Physiology* and *Insect Biochemistry*; a number of other publications also take



work in this area. It seems unlikely that there are enough good papers to keep another journal going, especially one aiming to be international. Perhaps this is why, within eighteen months of its initiation, the journal has gone from drawing its contributions from around the world to representation from the United States alone. I can't imagine that it will make much headway in many countries outside North America, but maybe it's not meant to, since only five of the 31-strong editorial board come from outside that continent. This is the American house journal of insect physiology and biochemistry. □

J. F. V. Vincent is a Lecturer in the Department of Pure and Applied Zoology, University of Reading, Whiteknights, Reading RG6 2AH, UK.

Routes to renewal

Alan Brafeld

Experimental Biology: Environmental and Sensory Aspects. Editor-in-chief M.A. Ali. Springer International. 4/yr. DM 170, \$61.

Zoological Science. Editor-in-chief Nobuo Egami. Zoological Society of Japan/VNU Science Press. 6/yr. Surface DM 411, air DM 434.

WHEN a journal starts to look jaded, the editors can either change its title and modify the content to increase its appeal, or they can merge with a similar journal, gaining strength from the union. Here is an example of each policy.

La Revue Canadienne de Biologie Expérimentale, founded under a slightly different name in 1942, became *Experimental Biology* last year, reflecting a change in publisher from the Université de Montréal to Springer-Verlag. Volume number sequence has been maintained, so the first volume of *Experimental Biology*,

for 1984–1985, is number 43. The four numbers comprising this volume, about 300 pages in all, contain 21 original articles and two review articles. The use of "biology" in the title is inapt, if this volume proves typical, for there are eight papers on mammals (including man), seven on other vertebrates and five on microorganisms; but only two concern invertebrates and only one plants. Of course this doesn't



matter once you know — the *Journal of Experimental Biology*, after all, is solely concerned with animals. Ali writes in an introductory editorial: "While the editors will consider any article in experimental animal and human biology in a wide sense, an attempt will be made to orient the journal towards environmental and sensory aspects of experimental zoology and medicine". This policy should succeed in time, but about half the papers in Vol. 43

deal with areas of cell biology or biochemical physiology which have no obvious relevance to either environmental or sensory aspects.

All the papers are in English and seem of a good standard, and the editorial board is drawn from nine countries. The production is of the high quality we expect from Springer. Promised publication time is about six months, but as the papers do not carry acceptance dates one cannot see how often this aim is fulfilled. There is a comprehensive and valuable book review section (and also a long list of books received) in three of the four numbers.

Zoological Science has been born of the marriage between the two official journals of the Zoological Society of Japan: *Zoological Magazine*, which was published in

ZOOLOGICAL SCIENCE

Japanese and first appeared in 1888, and *Annotationes Zoologicae Japonenses*, which started nine years later and carried papers in Western languages but had rather a limited distribution. Volume 1 of *Zoological Science* appeared in 1984, with six bimonthly numbers amounting to over a thousand pages. (This is more than three times the size of *Experimental Biology* at less than three times the price.)

The new journal is an attempt to bring Japanese zoological research before a wider international audience, and it certainly deserves to succeed in this. All the papers are by Japanese but all are in English, and a wide yet well-focused view of Japanese zoology emerges. Each issue available to me contains two reviews and 15 or more original papers (some being short communications). These are conveniently grouped on the contents page in subject areas: physiology, cell biology, biochemistry, genetics, developmental biology, endocrinology, behaviour, taxonomy. The quality of the papers is high and the production excellent. One of the numbers of Vol. 1 is devoted to several hundred very short abstracts of the papers presented at the annual meeting of the Zoological Society of Japan, and this is to become the standard practice.

In short, I have reservations about *Experimental Biology*, which has not yet developed the distinctive flavour it is seeking. On the other hand, it is clear from the outset that *Zoological Science* will prove an extremely valuable addition to our libraries. □

Alan Brafield is Senior Lecturer in the Department of Biology, King's College London (KQC), Campden Hill Road, London W8 7AH, UK.

Journal prices

Details of editors and frequency of publication, and the subscription rates appearing at the top of each review, are given in most instances for 1986. This information is not complete in all cases, and readers interested in subscribing to a particular journal should check the rates with the publisher concerned.

Little considerations

Keith Dumbell & Denise Roditi

Microbiological Sciences. Editor-in-chief C. M. Brown. *Blackwell Scientific*. 12/yr. UK £110 (institutional), £37 (individual); North America \$145 (institutional), \$45 (individual).

The Antimicrobial Newsletter. Editor Daniel Amsterdam. *Elsevier, New York*. 12/yr. North America \$55, elsewhere \$76.

Microbiological Sciences has been published monthly since April 1984 under the auspices of the International Union of Microbiological Societies (IUMS), whose newsletter it has supplanted. IUMS represents 80 societies in 57 countries and therefore caters for the needs of microbiologists practising in advanced and developing countries, in all branches of the science. The journal is intended to be affordable and widely read, and help microbiologists to keep aware of progress in

MICROBIOLOGICAL SCIENCES

the too easily separable branches of their subject. Broadly, then, it aims to do for microbiological scientists much what *Nature* and *Science* do for scientists in general.

Each issue carries four or five review articles on specific topics, a series of brief notes, book reviews and a calendar of forthcoming meetings. Most issues also have a centre-page chart, diagrammatically summarizing things such as the genetic map of *B. subtilis* or the structure and properties of immunoglobulins.

There is, it seems to us, a basic flaw in this approach. Microbiology is not a self-contained science, and its knowledge base and specific methodology account for only a part, often a small part, of the microbiologist's needs. Those microbiologists engaged in medicine, industry and agriculture may be more interested in keeping abreast of developments in biochemistry, genetics, pathology or botany than in progress in branches of microbiology other than their own. Should the need arise to consult a review on viroids or yeast genetics or crown gall bacteria, there are specialist journals where articles of this sort can be found. *Microbiological Sciences* is too slim to serve as an overall reference source, and while many good reviews have appeared, too high a proportion of them concentrate on extending the reader's stock of facts. Surely it would be better, in a journal such as this, to adopt a more synthetic approach, with the main emphasis on conceptual and methodological innovations?

There is no doubt that IUMS needs a forum for communication and the editors of *Microbiological Sciences* have prom-

ised to react to feedback from readers. Although the early issues have been too ambitious there is hope that this young journal will settle down to a more realistic and useful *modus operandi*.

The *Antimicrobial Newsletter*, by contrast, is produced for a clearly defined and more limited readership among laboratory workers and physicians whose concern is with infectious disease. Even in this much narrower context there is still an abundance of data to be digested and a plethora of publications to be scanned, so it is cheering to find a well-written journal that provides concise reviews on the subject. The presentation is enhanced by useful tables, clear diagrams and comprehensive references, although sometimes it could be improved by short editorial comment to resolve apparent discrepancies.

Each slim, seven-page issue contains one major article and up to two shorter pieces. For this the cost may seem excessive, but it is refreshing to be able to pick up a small journal and add so quickly and painlessly to one's knowledge. The pleasure is partly due to the absence of advertising — not a bad thing, considering the subject matter, and worth paying that little extra to enjoy. *Antimicrobial Newsletter* will be a welcome addition to any clinical microbiologist's library. □

Keith Dumbell and Denise Roditi are consultants in the Department of Medical Microbiology, Medical School, Observatory, Cape 7925, South Africa.

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Mixed agricultural produce

J.B. Owen

Research and Development in Agriculture. Chief editor C.T. Whittemore. *Longman*. 3/yr. UK £45, North America \$90.

THIS new publication fills a gap in the literature on agriculture between the established journals, which concentrate mainly on the research side, and the multitude of more ephemeral materials covering the development end of the spectrum. As far as can be assessed from the four numbers available for review, the practice lives up to the theory of the editor's objectives as expressed in the first issue.

The pattern of content developed thus far is a useful mixture of reviews with a core of papers, not commonly found in

RESEARCH AND DEVELOPMENT IN AGRICULTURE

other journals, dealing with such topics as modelling and surveys. In the systems modelling field, for example, contributions vary from discussion of principles to the exposition of the features of a particular model of sheep production and its application. Some, more conventional papers describing experiments in the development arena have also appeared.

Each issue, of some 60–70 pages, contains about eight articles and a book review section, the technical contributions ranging from longish reviews to shorter papers of five pages or less. The quality of the contents is properly enhanced by an attractive yet functional style of presentation, with adequate figures and tables.

Research and Development in Agriculture has set itself a high standard in the opening issues. It will have a secure future if it can maintain its initial momentum, appeal to a general readership and attract the busy young authors working in this thriving area. Appropriately, it has already published some overseas contributions, such as an economic analysis of research and development priorities in Mexican pig production, but one would expect to see the geographical scope expanding further from its Edinburgh base as the journal achieves wider recognition.

For the future, the editors might consider a regular "matters arising" section. Potential authors would also welcome an indication of the time between receipt and publication of manuscripts. □

J.B. Owen is a Professor in the Department of Agriculture, University College of North Wales, Bangor, Gwynedd LL57 2DG, UK.

Food for a science

Ian Morton

Food Microbiology. Editor B.H. Kirsop. *Academic*. 4/yr. UK £48, North America \$98 (for 1985).

International Journal of Food Microbiology. Editor-in-chief H. Sogaard. *Elsevier*. 6/yr. Dfl.274, \$94.48.

DURING the past few years, attention in food microbiology has been directed not only to the identification and quantification of food poisoning organisms (or their toxins) but to changes in the composition of the bacterial population by external means. These two new journals reflect this broadening of the subject, and have other points in common: both were launched at the beginning of 1984, and both have an international editorial board.

In *Food Microbiology*, we have in each issue an interesting and provocative editorial together with a correspondence section. The editor clearly states his intention that not only will original papers be considered by the journal, but also "state of the art" reviews will be published, along with book reviews. These aims have been met successfully in the first year. Original papers dealing with *Clostridium perfringens* and also *Campylobacter jejuni* have appeared, as has a bacteriological survey of water and ice for general uses in Thailand. It is stimulating to read reviews such as this, and to realize that food micro-

biologists are becoming aware that they must take into account a multitude of factors bearing on their science. It is good, too, to see that when strains used for biotechnological processes are described, they must be made available to colleagues.

International Journal of Food Microbiology, an official publication of the International Union of Microbiological Societies and the International Committee on Food Microbiology and Hygiene, is a more traditional research-paper journal. The standard of refereeing is clearly high and the papers deal with bacterial and mould species of considerable interest to the food scientist; for example *Yersinia* species are described in various pork products and a number of papers deal with different *Campylobacter* species. The contributions cover a wide range of food products, ranging from fish and oysters to milk and yams.

With the stress now being laid upon food safety and prevention of food poisoning, both of these journals are likely to play important albeit differing roles. Despite the cost, any laboratory or teaching establishment at the tertiary level which deals with food and nutrition can ill afford to be without them. Food and drink are essential to life, and we should hope that food microbiologists will read the papers in these two journals and will play a full role in the development of their subject. □

Ian Morton is Professor in the Department of Food Science and Nutrition at King's College London (KQC), Campden Hill Road, London W8 7AH, UK.

Specialist sensation

A.G. Brown

Somatosensory Research. Editor Lawrence Kruger. *Guilford*, 200 Park Avenue South, New York, NY 10003, USA. 4/yr. North America \$75 (institutional), \$50 (individual); elsewhere \$90 (institutional), \$65 (individual).

Somatosensory Research aims to cover "the entire range of investigations related to somatic sensation and its neural mechanisms". It has a strong North American bias: 12 of the 22 members of the editorial board and 35 of the first 41 papers are from North American laboratories (14 of the papers from people on the editorial board). The first two volumes cover a wide range of subject matter, including electron microscopic immunocytochemistry, pathway tracing, electrophysiology and psychophysics. The papers vary wildly in quality, some being poor and others sound. Personally I found about 20 per cent of the contents of some interest.

The typeface is easy to read and the journal is produced on high-quality glossy paper. Line drawings are good but some half-tone illustrations leave a lot to be

desired (that may not be the fault of the publishers, as other half-tones are excellent). Unusually, there is no indication of when a manuscript was submitted or accepted. Such information I always find interesting, but more importantly without it intending authors have no way of telling how long it might take to have a paper published.

All of the contributions appearing in the first two volumes could have found a home in one of the established journals. Indeed, whether or not one thinks there is a subdiscipline of somaesthesia is a subjective matter. There would, perhaps, have been more sense in a journal of sensory research, covering the whole range, since cross-fertilization of ideas from one modality to another is of obvious importance. But, as the vision fraternity has long been divorced from the rest of us, this idea would probably be a non-starter.

This journal, then, is in the modern fashion of specialist publications, and provides a repository for research data in a rapidly expanding area. Unfortunately, what are needed are some unifying concepts in neuroscience, not further schisms.

A.G. Brown is Professor of Veterinary Physiology at the Royal (Dick) School of Veterinary Studies, University of Edinburgh, Summerhall, Edinburgh EH9 1QH, UK.

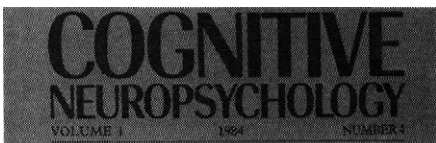
Meeting of neurology and psychology

Andy Young

Cognitive Neuropsychology. Editor Max Coltheart. Lawrence Erlbaum. 4/yr. UK £40 (institutional), £20 (individual); elsewhere \$60 (institutional), \$30 (individual).

ONLY 15 years ago psychology students were generally taught that the study of the problems experienced by neurological patients formed an arcane discipline, beset by logical pitfalls, that had little or no relevance to understanding normal experience and behaviour (though the study of brain-damaged rats and pigeons was, of course, quite a different matter).

When viewed against such a background, the increase in interest in neuropsychology has been remarkable. There have been many reasons why this has come about, but one has been the parallel between neuropsychological observations and some psychological models. The fashion in psychology is to conceptualize the cognitive system as being organized into separable processing modules. Modular systems will often have the property that their performance will break down in predictable ways, and these patterns of breakdown will in turn provide information on the nature of the processing modules themselves. This simple insight implies that the problems experienced by neurological patients are of interest to anyone trying to construct a psychological model to account for the performance of a



particular cognitive skill, and that such models can also be used to help in understanding patients' difficulties.

The exchange of theories and data between psychologists and neuropsychologists has become so fruitful that a journal devoted to this purpose must be welcomed. *Cognitive Neuropsychology* fits the requirements admirably. It publishes both theoretical and empirical papers, and it interprets "cognition" broadly, so that it is willing to consider papers on topics falling under headings as diverse as perception, attention, language, thinking, memory and action.

Cognitive Neuropsychology will be read both by experimental psychologists and by neuropsychologists. The work reported in the issues reviewed here is both interesting and first-rate. However, most of the papers are about language (13 out of 15 in the issues available for review). Although this is probably a fair reflection of the current high level of interest in language,

it is to be hoped that a better balance can be achieved in future.

The predominant research strategy used by cognitive neuropsychological researchers has been to carry out relatively detailed investigations of individual patients. As yet, however, few seem to have tried to take the additional step of arguing that an adequate theory should not only account for a patient's difficulties, but also make clear what (if anything) can be done to alleviate them. It is particularly gratifying to note that the editors of *Cognitive Neuropsychology* state that they will welcome reports of such work.

New neurobiology

Roger Keynes

Journal of Neurogenetics. Editor-in-chief R.N. Rosenberg. Elsevier. 6/yr. Dfl. 242, \$91.03.

Neuroscience Research: The Official Journal of the Japan Neuroscience Society. Editor-in-chief M. Ito. Elsevier. \$111 (institutional), \$55 (individual).

AT a time when it is commonplace to hear complaints about the ever-increasing number of journals, it is comforting to find one, the *Journal of Neurogenetics*, which seems set to fulfil its editors' motto: "it flies on its own wings".

With the application of the techniques of molecular genetics to neurobiology a profusion of studies is appearing, falling into two broad and overlapping areas: those which primarily deal with genetic factors or mechanisms, and those which are more concerned with using the techniques to investigate related areas, for example neurotransmitter receptors. The stated aim of the *Journal of Neurogenetics* is directed more towards the first of these, including "the genetic mechanisms underlying early embryonic development, cell differentiation, pattern formation and genetic disorders of the nervous system from microbes to man". That said, it was a little disconcerting to find in a recent issue an article on renal tubular acidosis. Generally, though, the journal sticks admirably to its brief, with articles ranging from analyses of *Drosophila* and *C. elegans* mutants to genetic counselling. Production quality is good, as is speed of publication, the delay being normally less than five months from date of acceptance.

As neurobiology differentiates into subdivisions such as neurogenetics, it can be argued that there is, more than ever, a need for eclectic journals which can provide a general view of the subject. A good recent example would be the *Journal of Neuroscience*, the publication of the American Society for Neuroscience. Perhaps not to be outdone, the Japan Neuroscience Society last year launched its own journal, *Neuroscience Research*.

Two other features of the journal deserve comment. The policy of encouraging book reviews that turn into interesting scholarly contributions in their own right is most effective, and the idea of reprinting historic papers that are no longer widely known (but deserve to be) is also commendable.

This, then, is a journal which has accurately identified the emergence of a distinct field of study, and will rapidly become indispensable to those working in it. □

Andy Young is a Lecturer in the Department of Psychology, University of Lancaster, Lancaster LA1 4YF, UK.

The journal's message is one of integration rather than fragmentation of disciplines. Its goal is a noble one — "the integration of various levels of our knowledge towards complete understanding of the brain" — and the intention "to be international in nature, serving neuroscientists throughout the world". The papers cover the entire range of neurobiology, with, in four representative issues, an interesting preponderance of neuroanatomy. Its success will inevitably reflect the success of Japanese neuroscience, whether or not it publishes papers from other parts of the world, and one can only wish it well. □

Roger Keynes is a Lecturer in the Department of Anatomy, University of Cambridge, Downing Street, Cambridge CB2 3DY, UK.

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Coverage

Clinical biomechanics is the application of the principles of classical mechanics to the solution of clinical problems. *Clinical Biomechanics* will explore its field from all aspects, although there will be an emphasis on contributions to the clinical management of mechanical dysfunction. The journal will cover aetiology, diagnosis, treatment and prevention, as well as rehabilitation. All therapeutic and investigative specialities involved in the management of musculo-skeletal ailments will be represented. The contribution of basic sciences is recognised and they also will be covered together with their applications, particularly in biomechanics and ergonomics.

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The biologist's eye on human affairs

Robert Attenborough

Biology and Society. Editor D.F. Roberts. *Eugenics Society*, 69 Eccleston Square, London SW1V 1PJ, UK. 4/yr. £14, \$27.

BIOLOGY and society interact in many different ways, but *Biology and Society* concentrates on interactions involving human reproduction, genetics, demography and health. In this it differs from some similarly titled publications, but it does invite comparison especially with the *Journal of Biosocial Science*.

Modestly enlarged, and now with an editorial board, *Biology and Society* is the reincarnation of the *Bulletin* of the Eugenics Society. The *Bulletin*, which did not attempt to be a major research journal (unlike the *Journal of Biosocial Science*), acted mainly as the Society's internal forum for news and discussion. *Biology and Society* has taken over this domestic role, and a large proportion of its space is devoted to editorials, lecture texts and summaries, conference notices and reports, the Society's news, book reviews and notes on articles in other publications.

The journal is, in other words, something of a hotchpotch. Quite a few of the main items, such as commentaries on the Warnock Committee Report and the Mexico City Population Conference, are substantial, balanced and interesting. Many of the smaller pieces too, including book reviews, are well worthwhile. But certain contributions, including a disappointingly unincisive lecture by a former British Cabinet Secretary, seem less commendable. And some minor entries, such as the less detailed conference reports where we learn little more than that so-and-so spoke on the subject of such-and-such, are unlikely to be useful beyond a limited circle.

Unlike its predecessor, *Biology and Society* also publishes research reports, and in this respect its role seems less clearly differentiated from that of the *Journal of Biosocial Science*. The reports in *Biology and Society* are generally shorter, but their range of topics is similar, and the need for a new outlet is therefore not obvious — unless it is a matter of sheer volume. Nonetheless, some interesting papers have appeared, for example on smoking, genetic counselling, infertility and infant mortality.

The journal, especially in its new form, is evidently trying to appeal to readers beyond the Eugenics Society, and the major institutional libraries needing to cover this field will wish to subscribe. But in two particular respects, its role seems not (yet) to be clearly defined, which may discourage less committed libraries and individuals. The first is that the Society's

objectives beyond the support of academic research are stated in very general terms — who could disagree with the aim of fostering "a responsible attitude to parenthood", for example? — so that outsiders can be forgiven for uncertainty about the extent to which Francis Galton's intellectual legacy weighs on the journal's shoulders.

The other problem concerns the nature of the intended audience. In its emphasis on news and topical discussion, often non-technically presented, it sometimes seems to seek an audience beyond academia (as *Anthropology Today* does in contrast to the more specialist *Man*). Indeed the potential for such a role is very real. At other times, however, both content and style are more specifically academic. So different parts of the journal appeal to different readers: but then — though their place in the market is vastly different — the same may be said of publications such as *Nature*. □

Robert Attenborough is a Lecturer in Biological Anthropology in the Department of Prehistory and Anthropology, A.D. Hope Building, Australian National University, GPO Box 4, Canberra, ACT 2601, Australia.

Technology in time

Colin A. Russell

History and Technology: An International Journal. Executive Editor Pietro Redondi. Harwood. 4/yr. North America \$70 (corporate), \$60 (institutional), \$30 (individual); UK £58 (corporate), £50 (institutional), £25 (individual).

"THE development of gadgets" is one way to describe the history of technology. It would not, however, please the sponsors of this new journal. In the following rather grandiose terms the editor states his objective:

We wish to see technology through its relationship to history by placing it at the center of historical perspective as a variable that is autonomous without being independent of the state of society.

Which means (I think) that he intends to take a hard look at technology in its social context. This is a laudable ambition. Much that used to pass for history of technology was almost entirely insulated from all other kinds of contemporary history. As with the history of science in the past few decades, this "internalist" approach is widely seen today as restrictive, artificial, arbitrary and rather pointless. Merely assembling data on the machine as it has changed through the ages is rather like stamp collecting: fun (if you like it) but of little intellectual content or explanatory power. Another way of putting it is to say that, if history of technology may be properly located within technology itself, then it is equally appropriate to regard it as part

of history. *History and Technology* appears to be trying to do just that and, indeed, to make technology a central theme in history, relating it to all kinds of other trends and happenings.

These concerns are reflected in the journal's format. Four kinds of article are promised. Under "Foundations and Methods" are articles on methodology — what historians love to call historiography. "Studies" include specific case histories of technical innovation as well as collective and individual biographies "free from any hagiographical temptations". "Sources" deal, as expected, with documentary sources (in which are curiously included instruments and machines). Finally, "Notes" will communicate news of meetings and programmes, and report upon other initiatives in the subject.

The first two issues followed this format fairly closely with some general reflections on the nature of history and technology, studies on the steam engine in late-nineteenth-century France and on mechanics, thermodynamics and locomotive design. The combined third and fourth issue deals with one special theme: technology and economic crises, ranging from the great depression in the Middle Ages, through the Paris Exhibition of 1881 to the American slump of the 1930s. It also includes theoretical discussion on the relation between economics and technical progress, based on a critique of Marx and Schumpeter.

It would be unjust to suggest that *History and Technology* has the field to itself. An obvious rival is *Technology and Culture*, though this is more American than the new journal which has a strong European input, especially from France. At the price (Vol. 1 contained 341 pages) it is not outrageously expensive but neither is it cheap.

More pertinent is the question of its intended readership. For those seriously interested in the social history of technology, with an eye to finely judged historical argument, it will be a welcome addition to the periodical literature. If, however, the editorial board wish to address their journal to working scientists, engineers and the like they would do well to look to their house-style. Some of the literary infelicities in the first volume may be attributed to problems of translation. Others, however, are merely the verbal detritus of a new professionalism, an inevitable consequence of which is the development of an in-language. If some of the authors could be persuaded to avoid quite so much sociological and historical jargon their valuable insights would be available to a far wider audience. For an international journal with the exalted aims of this one, that would be no bad thing. □

Colin A. Russell is Professor of History of Science and Technology at the Open University, Walton Hall, Milton Keynes MK7 6AA, UK.

Outside emissions

John Fremlin

Journal of Environmental Radioactivity: An International Journal. Editor M.S. Baxter. Elsevier Applied Science. 4/yr. UK £60, elsewhere £65.

ALTHOUGH many periodicals will take articles on environmental aspects of radioactivity, there is a good case for a journal specifically concerned with the subject. Now we have one, *Journal of Environmental Radioactivity*. Most of the papers published to date are naturally concerned with radioactive pollution from materials arising from nuclear bomb tests or from the nuclear industry. Good examples of such articles in the first five issues are those dealing with the determination of plutonium in sheep faeces as a sensitive indicator of deposition on vegetation, the behaviour of radiocaesium in Scottish coastal sediments and the take-up by salt-water organisms of effluents from Sellafield.

An especially promising feature of the new journal, however, is that over a third of the contributions has been concerned with natural radionuclides. Even in Britain, with the world's largest discharges of artificial radionuclides into the seas around the coast, the annual collective dose to the population from these sources is 500 times less than that from cosmic rays, internal potassium and natural local gamma radiation.

Two papers which I found particularly

interesting described measurements of the natural alpha-emitting nuclide radon-222, in one case arising from New Zealand geothermal power plants and in the other from phosphate fertilizer sludge in India. Neither of these represent a serious hazard, but the papers warrant a good mark for the journal since the potentially controllable radon isotopes oozing from the soil and lingering in the well-draught-proofed houses of Britain must be responsible annually for causing at least 400 times as many cancer deaths as the whole of the British nuclear industry. *Journal*

JOURNAL OF ENVIRONMENTAL RADIOACTIVITY

of *Environmental Radioactivity* has appeared at an appropriate time to attract the flood of new articles that ought to be published over the next decade on methods of sealing dwellings against the entry of radon.

Original contributions of 2,000 to 4,500 words (plus tables and figures), review articles and book reviews, notes and conference reports are accepted. The single letter so far published expressed opinions on articles published elsewhere. Text and line-diagrams are clear, there are no page charges and 25 offprints are supplied free. The subscription rate is not unreasonable and altogether the journal seems set for a healthy future. □

John Fremlin is Professor Emeritus of Applied Radioactivity, University of Birmingham, Birmingham B15 2TT, UK.

Matters of gravity

C.J.S. Clarke

Classical and Quantum Gravity. Editor M.A.H. MacCallum. Institute of Physics. 6/yr. North America \$215, elsewhere £135.

AT A time when many libraries are cutting back on acquisitions, doubts inevitably arise when the number of journals devoted to a particular speciality increases. For some time the community of general relativity theorists has been served by *General Relativity and Gravitation*. But this journal has never had the success it deserved, either in sales or contributions (the shortfall in high-quality contributions being due in no small part to the publisher's failure, as compared with competing journals, to give free offprints). Consequently, general relativity papers have been spread over many publications, with an increasing number going to *Journal of Physics A* (published by the Institute of Physics), until the point was reached when the Institute decided to hive them off into this new, separate journal, *Classical and Quantum Gravity*.

The high standards that prevailed before the split have been maintained, and the journal has acquired a particular strength in attracting and publishing a blend of contributions on supergravity, quantum gravity and classical relativity, a mixture which seems to have been carefully fostered by its editor, Malcolm MacCallum, and which sets the journal apart from the predominantly classical *General Relativity and Gravitation*. Supergravity is perhaps the largest single topic covered (coming to dominate the letters sections of some of the later issues), but there is a wide spread of other topics: canonical quantization, cosmology, asymptotic structure and exact solutions are all well covered, with a discriminating selection of a few papers on alternative theories of gravity. A useful book review section is included.

There is evidence that the journal is starting to woo some North American writers away from their traditional outlets. If it succeeds further in this then it is set to become the main vehicle for papers on general relativity and associated areas. □

C.J.S. Clarke is a Lecturer in the Department of Mathematics, University of York, Heslington, York YO1 5DD, UK.

Not entirely at sea

R.C. Selley

Marine and Petroleum Geology. Editor-in-chief D.G. Roberts. Geological Society of London/Butterworths. 4/yr. UK £124, Europe £136, North America \$245.

THE declared editorial policy of *Marine and Petroleum Geology* is "to provide a forum for the exchange of multidisciplinary concepts and techniques of direct relevance" to all concerned with these subjects. Though the journal is published jointly by a British learned society and by a British publisher it boasts an impressive international editorial board, the catholicism of which is reflected in the diversity of the papers that have appeared to date. The scope is broad both in geography and content. Among the contributions published in the five issues available for review, for example, are papers on sea-level changes of the US continental margin, seismic stratigraphy of the Santos Basin, Brazil, the geochemistry of the Kimmeridge clay of Dorset, reflected light microscopy of chitinozoa and the relevance of induced polarization to quantitative formation evaluation.

This list of topics shows that *Marine and Petroleum Geology* is far wider in scope than its title modestly suggests. Moreover it is more than just a vehicle for research papers. It also carries citations of current earth science literature in the form of reference lists divided into headings that include geology, geochemistry (organic and inorganic), geophysics and well logging, and petroleum engineering, platform technology, drilling and pipelines. The first two issues carried an "Underwater Information Bulletin" (sic). This has now been discontinued — perhaps too many readers drowned. Also included are book reviews, conference reports, patents reports, and a calendar of future conferences and symposia.

The editorial board has sensibly adopted a large page size of some 21 by 30 cm. This is essential to allow the satisfactory display of the seismic sections and geophysical well logs with which the journal abounds. Colour printing and folding pages are other features which help to justify the journal's cost — it comes dressed in a brightly coloured cover sure to appeal to younger, more impressionable readers.

One witnesses the appearance of yet another publication to be consulted with mixed feelings. Nonetheless *Marine and Petroleum Geology* will be essential reading not only for geologists and geophysicists dealing with offshore and onshore geology, but also for oceanographers, geochemists, palaeontologists and petroleum explorationists. □

R.C. Selley is Reader in Petroleum Geology at Imperial College, University of London, Prince Consort Road, London SW7 2BP, UK.

Ground under in the literature

C.T. Shaw

Mining Science & Technology. Editors C.O. Brawer and B.N. Whittaker. Elsevier. 4/yr. Dfl. 244, \$84.13.

IN THE editorial in the first issue of *Mining Science & Technology*, the editors state that the journal "caters for the ever-changing needs of the mining and minerals industries"; their aim is "to provide a forum for the mining industry to publish the results of new research, to describe changes and new developments in mining procedures, to review design considerations and regulations and to present interesting case examples"; and they hope to "cover all aspects of the extraction of solid mineral materials from the earth".

These are grandiose aims, which thus far have led to a rather unfocused journal. Moreover a number of established journals, particularly the transactions of the appropriate learned institutions, already provide just such a forum. *Mining Science & Technology*, it seems, will not cover any area not already served by an existing publication.

The journal is attracting contributions from all over the mining world, though most of them have come from the United Kingdom (fifteen), the United States (eleven) and Canada (six). Papers from seven other countries have been published. In the seven issues which I have seen, there is a strong representation of members of the editorial board in the list of authors; in only one is there no paper from this source. This is perhaps understandable, but when note is also taken that nine papers have emanated from Nottingham, where one of the editors is based, one gains the impression that the journal has not yet reached the crucial stage where it generates its own flow of material.

As regards content, about half of the contributions have been in the general



area of rock mechanics and strata control (22 out of 43, though three of these dealt with fill materials). The rest have covered a variety of topics of interest to the mining industry. The quality is patchy, and some of the papers have been little more than technical notes. Such notes are of course useful to the practising mining engineer, but there are other, better outlets for this sort of communication.

The journal indicates the dates of receipt and acceptance of papers, but it is not clear what the arrangements are for refereeing. The time between receipt and

acceptance in one case was as short as four days and there are a number at five days, which does not seem to imply a very vigorous review procedure. There has been a wide range of time between the receipt of the paper and its appearance — between four and fourteen months — but the average seems to be six to nine months. The standard of production, however, is high, with clear text and illustrations, and there is no advertising other than the occasional puff for other Elsevier journals; for the reader, this is no small advantage.

Generally, only research papers are published. There are occasional book reviews, but these appear infrequently and such intermittent coverage hardly seems worthwhile. Similarly there is often, but not always, a page entitled "Announcements" which has notices of forthcoming

meetings, but this again is very limited in content and there are other places where much more comprehensive information can be obtained. Finally, one issue has carried brief reports on recent conferences, but that struck me as little more than filler material serving no real purpose.

Despite these adverse points, *Mining Science & Technology* is clearly still settling in to the market and a little longer will be needed before it can be decided whether it will attract papers of sufficient standing to make it indispensable to a mining engineer's library. For the time being, then, judgement must be reserved. □

C.T. Shaw is Professor of Mining in the Department of Mineral Resources Engineering, Imperial College, University of London, Prince Consort Road, London SW7 2BP, UK

A cosmopolitan air

Robert A. Duce

Journal of Atmospheric Chemistry. Editors Paul J. Crutzen and Dieter H. Ehhalt. Reidel. 4/yr. Dfl. 216, \$76 (institutional); Dfl. 110, \$39 (individual).

INCREASING awareness of the impact of human activities on the atmosphere has recently led to a marked rise in research on atmospheric chemistry, on scales varying from the regional to the global. Changes in atmospheric composition can affect climate, human health, agriculture and water quality in complex and often poorly understood ways.

The *Journal of Atmospheric Chemistry* was initiated to publish research on the chemical interactions between the atmosphere and the solid Earth, the oceans and the biosphere. It is not concerned with air pollution problems on the local scale, but emphasizes the chemistry of the natural atmosphere and how it can be perturbed by human activities. The focus is upon studies of the composition and physical chemical processes in the atmosphere, on laboratory studies of atmospheric homogeneous and heterogeneous transformation processes, and on advances in instrumentation for the measurement of atmospheric composition.

At the time of writing seven issues had been published, with an average of six to seven papers per issue. This is an international journal, which is reflected clearly in an editorial board drawn from 14 nations. The editors have done an excellent job selecting the board; the scientific expertise gathered together here is broad and comprehensive, and the individuals are among the best in the world in their fields. Eighteen nations are represented among the authors of articles published in the first seven issues, further emphasizing the journal's non-parochial character, and among the contributors are some of the

world's leading atmospheric chemists (and not only members of the editorial board!).

To date only regular scientific articles have been published; while book reviews are accepted, none have been published yet, and there appears to be no provision for comments from readers on the contents of previous issues. Speed of publication is difficult to assess, since individual issues do not indicate the month of publication, but the delay appears to be a reasonable five to eight months. A further

Journal of Atmospheric Chemistry

attraction for prospective contributors is that there are no page charges.

There are two other journals which primarily publish atmospheric chemistry papers having a somewhat similar scope. These are *Journal of Geophysical Research — Atmospheres* (published by the American Geophysical Union) and *Tellus B* (published by the Swedish Geophysical Society). *Tellus B*, which has an emphasis on chemical and physical meteorology, was launched as part of the restructuring of *Tellus* at almost the same time that *Journal of Atmospheric Chemistry* began. To start two new international atmospheric chemistry journals almost simultaneously might appear both risky and unnecessary. However, so far the quality of papers has been good in both. With a rapid expansion of research to be expected over the next several years, I believe both journals have a good chance to succeed. □

Robert A. Duce is Professor of Oceanography and Director of the Center for Atmospheric Chemistry Studies, University of Rhode Island, Kingston, Rhode Island 02881, USA.

Close relationships

John M. Thomas

Journal of Inclusion Phenomena. Editors Jerry L. Atwood and J. Eric D. Davies. Reidel. 4/yr. Dfl. 236, \$84 (institutional); Dfl. 115, \$40 (individual).

INCLUSION complexes, like so many other materials and physico-chemical phenomena, were first identified in the Royal Institution, London, in the early years of the last century. Both Faraday, who reported the preparation of chlorine clathrate hydrate in 1823, and his mentor Davy worked on the complexes formed by the interaction of hosts and guests.

The *Journal of Inclusion Phenomena* reports original research on systems in which the hosts range from synthetic macromolecules through small heterocyclics to natural and synthetic minerals, and the guests from the atomic to molecular to ionic species. That host-guest systems are of immediate practical importance is self-evident: heterogeneous catalysis, especially that which involves zeolites, clays and graphites, is one example; chromatography and the electrochemistry of batteries and other energy storage devices are others. There are several more in the pharmaceutical world. And the whole realm of intercalation, involving inorganic hosts such as metal chalcogenides, or biologically important ones such as DNA, entails inclusion of one kind or another. At the fundamental level, inclusion phenomena offer abundant scope for the thermodynamicist, the preparative chemist, the quantum physicist and computer graphics enthusiasts.

With such a broad territory to cover there is little risk that this journal, unlike many of the ones that have been spawned so freely by publishing houses and their eager academic collaborators, will gradually retreat into a small enclave. By the same token, one wonders why, apart from commercial expediency, a new publication needs to be created when the standard outlets of learned societies are available to all concerned. These days, one should, in all conscience, question whether more new journals devoted to primary rather than secondary (review type) literature serve the best interests of the scientific community.

My scepticism about new journals is, in this instance, tempered by the commendable quality of the contributions that have appeared in the first three volumes. There has been a number of stimulating articles, but few have scaled the heights comparable to those reached in the evocative account of clathrates by the man who gave them their name, H.M. Powell. Powell tells us why clathrates should have emerged in 1939: they were not recognized as such until his famous paper on the complexes formed by β -quinol was pub-

lished in 1947. He also writes of his childhood courtship with crystals which started with "glittering pyrites in the local coal and [granulated] sugar on the table". His story encompasses the views of an aged widow of a Welsh quarryman on covetousness; the links between T.V. Barker (renowned for the once famous Barker index, now of blessed remembrance) and Fedorov; and the etymology of the word clathrate. To convey the notion of molecular imprisonment, Powell cites the word *clathri* (from *A Dictionary of Roman and Greek Antiquities*, 1884), which signifies a trellis or grating employed to cover and protect an aperture. He reminds us, too, that the Welsh word for burial ground is *claddfa*.

One can only hope that as well as assembling sound fact and serving as a means of promulgating the acknowledged scientific method of proof by repetition, this journal will also encourage articles possessing the scholarly charm and sweeping erudition of H.M. Powell's opening contribution. □

John M. Thomas is Professor in the Department of Physical Chemistry, University of Cambridge, Lensfield Road, Cambridge CB2 1EP, UK.

Just on the surface

John C. Vickerman

Adsorption Science & Technology. Editor Paul A. Sermon. Blackwell Scientific. 4/yr. UK £60, Europe £72, North America \$125.

Physics, Chemistry and Mechanics of Surfaces. Editor-in-chief E.P. Velikhov. Gordon & Breach. 24/yr in two volumes. Per volume: UK £546 (corporate), £464 (institutional), £232 (individual); North America \$656 (corporate), \$558 (institutional), \$279 (individual).

ADSORPTION is a crucial phenomenon in gas-solid, liquid-solid and gas-liquid systems, and there are few areas of technology which are not affected by the reactivity of surfaces in some way. In principle, therefore, a new journal entitled *Adsorption Science & Technology*, which claims to "welcome original papers dealing with adsorption theory, measurements and techniques" and "emphasises links between developments in these sciences to their practical and industrial applications", should be of considerable benefit to the scientific community.

The journal commenced publication in January 1984 with an excellent review on the kinetics of adsorption by Aharoni. Since then 30 research papers have appeared in the five issues to January 1985. In general the quality of the work reported is good and the acceptance times have been less than two months. The format and production are also good,

although the figures are inordinately large.

Despite these positive impressions, to me the journal seems to be only partly successful in meeting its aims. It is developing into the house publication for the physical adsorption fraternity. Twenty-two of the 30 papers published to date deal with this field; furthermore, of these 22, 16 come from only five research groups, one group having published seven. Most of the remaining papers are concerned with various aspects of chemisorption, and these could naturally have found a place in one of *Journal of Catalysis*, *Surface Science*, *Applications of Surface Science* or *JCS Faraday I*. Moreover there is little to suggest that the journal is realizing its goal of linking applications to the basic science. Thus it appears that *Adsorption Science & Technology* is attracting support from only a very narrow base, which casts doubts on its role and its ultimate chances of survival.

Physics, Chemistry and Mechanics of Surfaces is a cover-to-cover translation of *Poverkhnost'*. *Fizika, Khimiya, Mekhanika* of the USSR Academy of Sciences. Translations began in 1982, the first issue appearing in November 1983. Although a volume's subscription may seem expensive, it does cover twelve issues of some 300 pages each.

There is great value in this publication because it gives a detailed insight into Soviet surface science. It is well produced, clearly printed and in general the papers are of good quality and useful length. The ideal of bringing together research work on the physics, chemistry and mechanics of surfaces is very commendable — frequently a problem which seems puzzling to a physicist can be solved when the chemist's viewpoint is brought to bear and vice versa. However, despite the high aims, the vast majority of the papers deal with the physics of surface phenomena and the journal is not, I think, as catholic in its coverage as, for example, *Surface Science*.

There is considerable variation in the speed of publication, some papers taking only a few months, others up to two years (a helpful section reproduces the abstracts of forthcoming contributions). There is also considerable variation in the extent to which the Russian authors reference Western journals — some papers refer extensively to the non-Russian literature, others have wholly Russian citations. Whilst one can criticize the parochialism of the latter authors, it is well to remember that without translation journals such as this most Western scientists would be completely ignorant of the very valuable work being done in laboratories in the Soviet Union. □

John C. Vickerman is Senior Lecturer in Physical Chemistry and Senior Consultant to the Surface Analysis Service, University of Manchester Institute of Science and Technology, PO Box 88, Manchester M60 1QD, UK.

Package of products for the chemist

A. I. Scott

Natural Product Reports: A Journal of Current Developments in Bio-organic Chemistry. Chairman of the editorial board G. Pattenden. *Royal Society of Chemistry, London, UK. 6/yr. £130 (UK), \$252 (North America), £143 (elsewhere).*

IN 1970 the Royal Society of Chemistry launched *Specialist Periodical Reports* which reviewed the literature of natural products on an annual or biennial basis. This series has now been discontinued and its place taken by the new bimonthly journal, *Natural Product Reports*.

The range of topics has been broadened from the original *Reports* on alkaloids, terpenoids and steroids, biosynthesis, and aliphatic and related natural product chemistry to include occasional accounts of chemotaxonomy, enzymology, biotechnology and spectroscopic techniques. The literature is usually covered for a twelve-month period except in some of the more esoteric disciplines where a two-to-three-year review is intended. Although the time lag for each article published is about twelve to eighteen months, the value of this publication to natural product chemists, whether in a university or industry, is unquestionable.

All is not perfect, however. In any journal the style and approach of the contributors will vary, and *Natural Product Reports* is no exception. We are presented with the whole spectrum, from terse, rather conventional compilations of data to almost chatty and, at times, biased views of a given field. While a degree of latitude in style is acceptable, the swing from uncritical to extremely rigorous reviewing can be misleading to those readers who wish to get into one of the natural



product areas outside their current interests. Indeed, one hopes that some kind of gentle refereeing process will be applied to those articles (only one in the first seven issues) which bear the marks of a parochial view of the field.

Nevertheless *Natural Product Reports* is a most welcome arrival. The reviews are not only comprehensive, but all one needs to know about a given subject is conveniently packaged in one journal and there is every opportunity to sample the flavour of natural product structures other than those of one's own favourite class. The subscription price may seem steep, but the

collections of references and the clear structural formulae to be found in each issue are good value for money. Thus, many of the articles contain 250–300 structures, and the topics covered in the seven issues available for review include 14 classes of alkaloids, all classes of terpenoids (and steroids), rotenoids, macrocyclic microbial metabolites, marine natural products, insect pheromones, biosynthesis of polyketides, terpenes, shikimate metabolites, porphyrins, chlorophylls and corrins, synthetic chemistry and an analytical method (droplet counter-current chromatography). An author and subject index appears annually, and a running cumulative index of authors and titles of

their reviews is provided in each issue.

The editorial board is to be commended for producing a publication which will be of great value in helping the natural product chemist keep track of the novel structures which appear in the literature at the rate of one every 400 minutes. Moreover the journal also includes periodic reviews of those techniques which are revolutionizing the isolation and structural elucidation of the compounds of nature, a feature which many will find useful. □

A. I. Scott is Davidson Professor of Science in the Department of Chemistry, Texas A & M University, College Station, Texas 77843, USA.

Across the divide

Ian M. Mills

Soviet Journal of Chemical Physics. Editor-in-chief N.N. Semenov. *Gordon & Breach. 12/yr. UK £546 (corporate), £464 (institutional), £232 (individual); North America \$656 (corporate), \$558 (institutional), \$279 (individual).*

CHEMICAL physics in the Soviet Union has a wonderful parentage, in the eyes of Western scientists, through the remarkable series of monographs written by Landau and Lifshitz, which have been available in English translation from Pergamon Press for many years. These volumes, which comprise a complete "course in theoretical physics", are the most authoritative and comprehensive set of textbooks on the subject; they are useful both for teaching and for reference, and they set a high standard in every way. I see them as a shining example of the international nature of science, and expect to find a similarly high standard of chemical physics in the Soviet Union.

Yet the truth is that most of us know little of current efforts in this field in Russia, and there are few references to Soviet research in the Western literature. Is there good work being done there, but unknown to us in the West because of the language barrier? If so, this new journal, a cover-to-cover translation of *Khimicheskaya Fizika*, will be invaluable in helping to bridge the language and cultural gap between Western and Eastern scientists.

The English translation is nicely produced, in a small A5 page format, and covers some 3,000 pages per year; however it appears rather more than a year after the original Russian publication. The subject matter seems to span the full area of chemical physics, from the physics and chemistry of polymers, through electron tunnelling in chemistry, to molecular energy relaxation in gas discharges. Both theory and experiment are represented, with theory perhaps predominant (as is probably the case in Western journals).

Yet the papers have a dated look in comparison to those appearing in, for example, the American Physical Society's *Journal of Chemical Physics*; they tend to be shorter and more general than the papers we see in the West. Above all there is no evidence of the influence of computers: *ab initio* calculations, tables of numerical data and all kinds of high-resolution spectra are noticeably absent. The theoretical contributions tend to concentrate on the derivation and discussion of analytical formulae.

Another point of interest is the references. About a third of the papers cite

Soviet Journal of Chemical Physics

A COVER-TO-COVER TRANSLATION
OF KHIMICHESKAYA FIZIKA

only Russian work and the remainder have rather more Russian than Western references. It hardly seems likely that this reflects the proportion of research in the field, and one must conclude that the communication barrier is as great West to East as it is East to West.

This new journal must be welcomed as providing another channel across the divide, for those who can afford to pay the price (which seems high, even to our institution libraries). However looking through it leaves me with the impression that chemical physics in the Soviet Union is far behind similar work in the West, despite the heritage of Landau and Lifshitz. □

Ian M. Mills is Professor of Chemical Spectroscopy in the Department of Chemistry, University of Reading, Whiteknights, Reading RG6 2AH, UK.

Journal prices

Details of editors and frequency of publication, and the subscription rates appearing at the top of each review, are given in most instances for 1986. This information is not complete in all cases, and readers interested in subscribing to a particular journal should check the rates with the publisher concerned.

Washington's power supply collapse

from Roger H. Bezdek

The largest municipal default in US history is likely to influence public policy for the remainder of this century — not only in the power supply industry.

ON 25 July 1983 the Washington Public Power Supply System (WPPSS) defaulted on \$2,250 million of municipal revenue bonds. This, the largest municipal default in US history, will influence energy project development and financing, the municipal bond market and state and local government finances for the remainder of this century.

The default and its tumultuous aftermath generated a large amount of publicity and, over the past two years, much has been written on the "Whoops" fiasco. But most of what has appeared so far has been polemical and accusatory in nature, blaming the Washington State Supreme Court, the Bonneville Power Administration (BPA), public utilities, Wall Street investment companies, federal regulators, environmentalists and a host of others for the problem. Here we develop an objective assessment of the factors that led to the default and discuss some of the broader implications for the future.

Pacific Northwest

Over the past half century, the Pacific Northwest (Washington, Oregon and Idaho) has enjoyed electricity rates. Electricity costs have been approximately one-third to one-half of the US average, with the result that between 1976 and 1981, per capita electricity consumption in the region was 75 per cent greater than in the United States as a whole. Over the period 1980–82, when average US residential tariffs were rising at 16 per cent a year, the average cost of electricity in the Pacific Northwest for urban households consuming 500 kWh per month increased much more slowly¹.

Several factors contributed to these relatively low electric rates. Since the late 1930s, the Pacific Northwest has enjoyed a surplus of electrical power and, over the past five years, the power generated has been 10 to 20 per cent in excess of sales. In addition the BPA exchange programme makes low cost power from BPA available to residential and small agricultural customers of investor-owned utilities.

Historically, however, the most important factor underlying the Pacific Northwest's low electricity rates has been its access to hydroelectric power, which provides nearly 90 per cent of the region's power, compared with 14 per cent for the United States as a whole. Although hydroelectricity is inherently an efficient and inexpensive means of power generation where conditions permit, the major

reason for the cost advantage of hydroelectric power over fossil and nuclear power, especially in the Pacific Northwest, is the heavy federal subsidy of hydroelectric facilities (see ref. 2).

Bonneville

The Bonneville Power Administration was established in 1937 to market power from the Bonneville Dam and, thereafter, from the Grand Coulee Dam on the Columbia River. Before 1937, private utilities had failed adequately to serve rural areas and, as a result, Congress sought to encourage the development of public utilities and cooperatives by giving them preference in the allocation of power from federal hydroelectric facilities³. BPA at present markets power from 30 hydroelectric projects with a capacity of nearly 20 million kW, and its transmission system includes 363 substations and more than 13,200 miles of transmission lines. BPA is thus analogous in history, scope and function to the Tennessee Valley Authority.

BPA's authority has rapidly expanded beyond its original mandate. During the Second World War, it began to transmit (or "wheel") private and other public power, which led to the formation of the Northwest Power Pool consisting of ten utilities connected to the federal transmission grid. In the 1950s, Congress designated BPA as the marketing and transmitting agent for power produced at a number of newly constructed dams³. Following a treaty with Canada in the early 1960s, providing for the coordinated operation of each country's dams on the Columbia River, BPA and other members of the Northwest Power Pool entered into a new scheme to market surplus power generated at different seasons.

In the late 1960s, there began phase I of the ten-year Hydro-Thermal Power Program (HTPP), designed substantially to increase the power-generating capacity of the Pacific Northwest. Although still not authorized to acquire or own generating facilities, BPA agreed to help finance the construction of power plants through the purchase of their generating capacity. BPA's participation, through complex contractual arrangements known as net-billing, was sanctioned by Congress⁴.

The generating capacity of the Pacific Northwest, however, still fell short of demand. In late 1973, BPA and the utilities agreed to embark on Phase II of HTPP, the construction of eight more thermal plants and the expansion of the transmission system. The parties were to maintain

essentially the same roles as before, except that net-billing would not be used.

With the passage of the Federal Columbia River Transmission Act in 1974, Congress designated BPA as the marketing agent for all electric power generated by federal power plants in the Pacific Northwest. The act also made BPA the only power-marketing agency responsible for its own financing. This legislation gave BPA the authority to deposit its revenues in a revolving fund and to make expenditures to finance its operations. Significantly, it thus removed BPA from the annual congressional appropriation process.

During the 1970s, it still appeared that BPA would be unable to fulfill its commitments, and in 1976 BPA formally gave notice that power supplies could be reduced or terminated in the future—an action which provoked considerable controversy. BPA requested that Congress should resolve the question of power allocation and facilitate the coordinated planning of power development in the Pacific Northwest. In response, Congress enacted the Pacific Northwest Electric Power Planning and Conservation Act of 1980, which made major changes in BPA's authority and in the allocation provisions of the earlier statutes. BPA can now acquire energy resources on a long-term basis, with first priority for energy conservation and renewable resources.

Washington

The Washington Public Power Supply System (WPPSS) is a municipal corporation and a joint operating agency of Washington State which originally consisted of 23 publicly owned utilities. It was established in 1957 to construct dams and power plants. In 1968, with the active encouragement of BPA, it embarked on an ambitious programme of nuclear power development, announcing plans for the construction of three nuclear generating facilities—plants 1, 2 and 3. Two years later, WPPSS decided to begin construction of two further nuclear facilities, plants 4 and 5. These decisions were based on regional forecasts by the Pacific Northwest Utilities Conference Committee (PNUCC) and were in turn based upon individual forecasts prepared by every BPA preference customer and each investor-owned utility, together with a forecast of direct-service industry loads by BPA. The forecasts reached the ominous conclusion that, by the mid-1980s, the Pacific Northwest would be facing serious energy shortages with attendant dire con-

sequences for the region's economic development⁶.

The financing of each of the plants involved complex contractual arrangements between WPPSS, participating utilities and, for plants 1, 2 and 3, BPA. The arrangements were designed to ensure the security of the debts incurred by WPPSS for construction of the power facilities and, for nearly a decade, WPPSS enjoyed almost limitless access to the bond market⁷.

WPPSS plant 1 is located near Richland, Washington, on the Department of Energy's (DOE) Hanford Reservation and was designed to have a generating capacity of 1,250 MW. By the spring of 1982, the plant was 67 per cent complete and was due to come on line during the summer of 1986. In April 1982, the WPPSS Executive Board, on the recommendation of BPA, approved a delay in construction of up to five years; this delay has been extended indefinitely. Plant 2, with a designed generating capacity of 1,100 MW and also on the Hanford reservation, began commercial operation in December 1984. It is the only one of the five WPPSS nuclear power plants that is likely to become operational in the foreseeable future.

Plant 3, near Satsop, Washington, is designed for 1,240 MW and was about 75 per cent complete in May 1983, when work was suspended for three years, a suspension which is now indefinite. Plant 4 is on the Hanford reservation and was intended as a twin to plant 1. Plant 5 is near Satsop and was to have been a twin to plant 3. In January 1982, construction on both of these plants was terminated.

When construction began on these five nuclear power plants, the total cost was estimated to be approximately \$7,000 million. By 1981, the estimated completion costs were already in excess of \$23,000 million. By the time WPPSS terminated construction on plants 4 and 5 in 1982, their estimated completion costs had increased from \$3,500 million to \$12,000 million⁸.

The decision of the Washington State Supreme Court, on 15 June 1983, that 28 of the 88 participants in projects 4 and 5 did not have the legal authority to enter into take-or-pay contracts, left WPPSS without means of servicing the \$2,250 million in debt that had been issued. This court decision led directly, one month later (on 22 July), to the WPPSS default on \$2,250 million in bonds for plants 4 and 5, the largest municipal bond default in US history.

Default

The debate over responsibility for the default of the WPPSS will continue for many years, and is unlikely ever to be completely resolved.

It is clear that the load forecasts used in planning the WPPSS projects seriously overestimated future energy require-

ments. Until the late 1960s, nearly all electric power consumed in the Pacific Northwest was obtained from the region's hydroelectric resources. By that time, however, the baseload capacity of the existing resources was at or near its limit, and it appeared necessary⁹ to develop other sources. The association of 155 publicly owned and investor-owned utilities and consuming industries (PNUCC) estimated in 1968 that the annual load growth in the region would be approximately 7 per cent, as it had been during the 1960s, and predicted that there would be excess demand for electrical power by the late 1980s.

BPA assumed a central role in planning for the region's potential power needs during this period, even though prevented by its statutory authority from owning power-generating facilities¹⁰. BPA engaged in complex contractual arrangements in order to exercise its statutory authority to "acquire" but not own a resource. The plan, agreed upon by BPA and the utilities (HTPP), adopted in 1968 by PNUCC and approved by Congress in 1969, was to construct additional thermal-nuclear plants (up to eight) to augment baseload generating capacity. Although the plants were to be built by the utilities, BPA was to participate in paying for them through net-billing arrangements.

Phase I of HTPP began in 1971 and included nuclear power plants scheduled for commercial operation at various times during the 1980s (WPPSS plants 1, 2 and 3). Projections of the demand for electric energy suggested that the ten-year HTPP would not meet the region's energy needs, with the result that in 1973, Phase II of HTPP was adopted, calling for eight more thermal plants. WPPSS began construction of plants 4 and 5.

Representatives of the utilities testified in February 1983 that they had never been anxious to assume the risks involved in nuclear power development, and that they were persuaded ("coerced") by BPA¹¹. They claimed that BPA's 1976 "notice of insufficiency" had frightened local officials into approving construction of plants 4 and 5. But many observers reject this argument as self-serving, noting that little opposition to the proposed plants was voiced during the public hearings before the signing of the agreements, and that the utility representatives were members of a committee that met regularly and frequently throughout the construction period. Nevertheless, it is clear that the notice of insufficiency strongly influenced the decision to build plants 4 and 5; the alternative was held to be economic stagnation in the region.

WPPSS was ill-prepared to build one nuclear power plant, much less five. Most of the 23 members of the WPPSS board were farmers or small businessmen, with little or no experience of nuclear power, and included the owner of a muffler

(motor-car exhaust) shop, a veterinarian, the proprietor of a refrigeration company, a wheat rancher and the owner of an apple orchard. WPPSS used three different designs for the five projects, which suffered from repeated delays and huge cost overruns. Like other nuclear power plants, the WPPSS projects faced costly and continually changing government regulations caused by increasing public concern about the safety of reactors and the growing strength of the anti-nuclear power movement.

The system was also required to follow all Washington State rules and regulations, including a law that required contracts to be open to competitive bidding. The result was that some 500 companies and their 20,000 employees worked, frequently out of coordination, on and around the construction sites. WPPSS also had continual "problems in management", and work "was not being performed as efficiently" as it should have been¹². The end result was a sixfold increase in costs.

Another aspect of WPPSS financing, called capitalization of interest, has so far received relatively little attention, but is the reason why the system's problems came to a head only in 1982 and 1983. Until 1982, the participants had never really had to pay anything. According to James E. Spiotto, a recognized expert on municipal bond defaults¹³: "They capitalized for four, five, six years. They would do an issue. Part of the bond issue proceeds would go to construction. The other part would go to pay debt service built up over this period of time. They'd keep on doing issues, which would pay the debt service on previous issues and pay some of the construction costs." On the other hand, participants in the projects backed by netbilling paid interest before 1982.

The success of financing by this capitalization of interest accrued depended on the ability to continue to raise loans in the capital markets. When the cost reached \$5,000 million and the commercial operation of the plants had receded five years, far greater amounts of capitalized interest were needed than had been anticipated. It can be argued that the capitalization of interest is not a prudent financial practice in that if a project either produces no revenue or insufficient revenue, there will be inadequate funds to service the debt. The beginning of the end came when Robert Ferguson became managing director of WPPSS in 1980, and ordered a complete financial review. The resulting study showed that completion costs were approaching \$24,000 million and that it would be necessary to raise an impossible \$3,000 million in the financial markets within 12 months¹³.

Further to complicate the system's problems, while project costs were increasing and construction schedules lengthening, the predicted power shortages in the region were evaporating. By the early

1980s, when on the basis of forecasts made barely a decade earlier the region was supposed to have been on the verge of a debilitating energy shortage, the Pacific Northwest actually had a surplus of electrical power. The dire predictions of power shortages by the mid-1980s were, essentially, extrapolations of the seven per cent average annual growth in electricity demand during the 1960s and early 1970s. Well into the energy crisis of the 1970s, few analysts in the Pacific Northwest (or anywhere else) anticipated the dramatic effects that the price shocks of 1973-74 and 1979-80, and the consequent recessions, would have in inducing energy efficiency and conservation measures.

These effects were particularly significant in the Pacific Northwest. The region had traditionally enjoyed electricity rates about one-third of those elsewhere, with the result that the uses of energy in the region were notoriously inefficient. But these energy consumption patterns also implied that the potential for energy savings from relatively simple and inexpensive measures was very large. In addition, the recessions had an especially harsh impact on the region, further depressing growth in energy requirements¹⁴. Thus the stage was set for the financial and legal consequences to run their course.

Through net-billing arrangements, BPA had contracted to acquire the total capacity of WPPSS plants 1 and 2 and 70 per cent of the capacity of plant 3. BPA is obligated to pay debt service on the bonds issued to finance the construction of these plants, but it has no obligation for the costs of plants 4 and 5. BPA's obligations include the payment of the debt service, whether or not the net-billed plants ever become operational. The net-billing arrangement provides security for the debt issued so far by WPPSS for the construction of plants 1-3.

The concept of "acquiring" a resource must be distinguished from that of "owning" it. BPA is prohibited from owning power-generating facilities, but it is permitted to purchase the power-generating capacity of a facility. Net-billing is therefore a means for BPA to meet its statutory obligation of providing for the region's overall power requirements.

BPA's customers have in turn agreed to purchase shares of the output capacities of plants 1, 2 and 3 through net-billing contracts, and each participant is responsible for its share of the monthly debt service on the bonds issued by WPPSS. There are 104 participants in project 1; 94 in project 2; and 103 in project 3. The utilities that own 30 per cent of project 3 pay their shares of the monthly costs directly to WPPSS, not through net-billing arrangements, and thus do not contribute to the debt service costs of the bonds issued by WPPSS to finance the remaining 70 per cent of the costs of this plant. Debt service on these bonds is provided by the participants through the net-billing arrange-



Projects 1 and 4 of the Washington public power supply system — an idealized artist's impression.

ment. Under the net-billing contracts, each participant has agreed to assign its share of the electrical capacity of a project to BPA. In return, BPA has given the participant a credit equal to the cost of its share. Since the participant purchases electricity from BPA, the credit is applied against the amount due to BPA for power purchased.

The participant pays the amount of the credit directly to WPPSS, however, and is then billed by BPA for the amount it owes for power purchased—net of the credit. A participant failing to make its monthly payment to WPPSS loses its monthly net-billed credit, and the remaining participants in the project are assigned larger shares. Thus the net-billing arrangement effectively guarantees a source of funds for WPPSS to provide for debt service even if one or more of the participants should default⁶.

From the investor's perspective, the net-billing arrangement is an attractive means of providing security on the bonds issued to finance projects 1, 2 and 3. Its effect is to reduce revenues due to BPA from the participant by the amount required for debt service and construction costs. The funds required for debt service on bonds issued by WPPSS do not become available to BPA for its other financial obligations. The validity of the net-billing agreements was upheld by the Oregon Federal District Court on 28 April 1983 (see ref. 15).

The usefulness of the net-billing arrangement was nevertheless limited by Internal Revenue Service regulations issued in 1972. The regulations, which held that the federal government was no longer a tax-exempt agency, are the underlying cause of BPA's disassociation from securities issued by WPPSS for plants 4 and 5. They provide that obligations issued by a state or local government agency generally constitute taxable industrial development bonds if the obligations are secured by net-billing arrangements. Because WPPSS did not want to lose its tax-exempt status, the net-billing arrangement was superseded by another.

The financing arrangements for plants 4 and 5 do not involve BPA, and WPPSS sold nearly all of the generating capacity to 88 municipal corporations and cooperatives. Construction was financed by bonds

sold by WPPSS and backed by "take-or-pay" contracts (facetiously known as hell-or-high-water contracts) under which the participants agreed to pay specified shares of the costs of construction (including debt service) directly to WPPSS, whether or not the projects were completed. Take-or-pay contracts are commonly used to back debt issued to finance the construction of large power generating facilities and, as applied to plants 4 and 5, were not viewed with undue suspicion by any of the parties involved or by the bond market^{7, 13, 16}. When a power generating project involves greater risk than a single utility desires to assume itself, a take-or-pay agreement bringing together a number of utilities to share the risks has traditionally been thought reasonable.

Even so, the opinions of the reasonableness of these arrangements were not universally shared. When plants 4 and 5 were terminated in early 1982, many citizens of the Pacific Northwest were outraged at the prospect of paying off the bonds through several decades of higher electricity bills, with no hope of anything in return. Some utilities attempted to renege on their contracts. With the spectre of default on the horizon, the Chemical Bank, trustee for the holders of the bonds for plants 4 and 5, took WPPSS and the utilities to court.

After more than a year of legal manoeuvring, the matter reached the Washington State Supreme Court, which ruled, on 15 June 1983, that 28 of the participants in projects 4 and 5 did not have the legal authority to enter into take-or-pay contracts. This decision left WPPSS without means of servicing the debt on the \$2,250 million issued by that date. The court said:

Our conclusion is that Washington statutes authorize the participants to purchase power or to own electric generating facilities. An attempt to structure an agreement under the joint operating agency statutes or to base it upon implied powers does not alter the basic authority and the participants simply are not authorized to guarantee another party's ownership of a generating facility in exchange for a passive share of any electricity generated.

The chronology of legal actions leading up to default was as follows. On 28 December 1981, a group of ratepayers in Oregon filed suit to have the take-or-pay

contracts declared invalid. On 22 January 1982, projects 4 and 5 were terminated. Later in 1982, other Oregon and Washington utilities joined the suit, and the Chemical Bank then filed suit in King County (Washington) to force the participating utilities to honour the debt. On 27 January 1983, the Chemical Bank sued 11 Oregon utilities to force them to pay a portion of the debt. On 20 May 1983, the Chemical Bank asked the King County Superior Court to rule that the 88 participating utilities be forced to pay off the \$2,250 million in bonds. On 24 May, the King County Superior Court barred the Chemical Bank or the bondholders from putting WPPSS into default. On 15 June, the Washington State Supreme Court ruled that the local utilities are not obliged to repay the \$2,250 million. On 22 June the Chemical Bank attempted to have the restraining order preventing WPPSS default lifted. On 5 July, the King County Superior Court upheld the restraining order. On 22 July, the Washington State Supreme Court refused to reconsider its restraining order, allowing the Chemical Bank to declare a default and accelerate the bonds. On 25 July, WPPSS admitted in court that it had no realistic hope of repaying the \$2,250 million and was declared to be in default. On 26 September 1983, the Idaho State Supreme Court ruled that the participating Idaho utilities were not liable for the incurred debt, and on 7 February 1984, the Wyoming State Supreme Court ruled likewise for the Wyoming participant. On 6 November 1984, the Washington State Supreme Court, upon appeal, reaffirmed its decision of 15 June 1983.

WPPSS is now entangled in a legal morass. It is unlikely that the holders of the bonds for plants 4 and 5 will ever see more than a small fraction of the money they have invested. Perhaps the fitting epitaph for the "Whoops" experience was provided by Mark Reis, executive director of a Seattle energy-conservation coalition instrumental in bringing the issue before the Washington State Supreme Court: "They promised us power without cost, and they delivered cost without power."

Bond market

Anticipating the WPPSS default, some analysts pessimistically feared that interest rates would increase dramatically for new issues, that the secondary market would collapse and that investor confidence would plummet. A chain reaction of other defaults would then occur as projects could not be financed and take-or-pay contracts were invalidated elsewhere. Finally, regulatory authorities and elected officials would increase pressure for fundamental changes and the municipal bond market would be drastically altered. More optimistic observers held that if a compromise could be worked out quickly, probably with federal or state government assistance, WPPSS would then be regarded as a unique case which could not

happen again and the municipal bond market (the market for state and local government debt instruments) would return to normal.

The truth appears to lie between these extremes. WPPSS was not a disaster for either the municipal bond market or for the public power bond market, but a federal bailout never occurred. While an estimated 78,000 investors have been harmed and the negative publicity from the default has been immense, so far the impact of the WPPSS default on the tax-exempt municipal bond market (bonds issued to finance government power utilities are exempt from income taxes) appears to have been minimal, at least for the market as a whole.

In August 1983 the state of Washington sold \$150 million in general-obligation bonds, and the issuance carried an interest premium of only 75–100 basis points (a basis point is 0.1 per cent) because of WPPSS¹⁷. The claim that the WPPSS default has had a minimal impact on the tax-exempt market is evidenced by the successful sale, in September 1983, by the Michigan Public Power Agency (MPPA), an agency organized along the lines of WPPSS and with a comparable mission, of \$240 million in bonds backed by take-or-pay contracts with eleven Michigan utilities. The maximum yield on the bonds was set at 10.80 per cent, marginally higher (75 basis points) than the yields of comparably rated bonds¹⁸. Further evidence is provided by the fact that in November 1983 the utility with the largest stake in WPPSS plants 4 and 5, the Snohomish County Public Utility District No. 1, returned to the municipal bond market with an offering of \$243 million for a hydroelectric project and marketed the bonds with much less difficulty than expected. The bonds were priced to yield from 7.5 per cent for bonds maturing in 1986 to 11.75 per cent for bonds maturing in 2020, even though they carried ratings of Baa-1 from Moody's and BBB from Standard and Poor's (Moody's and Standard and Poor's are the two major firms that rate US bond offerings).

The effects of the WPPSS default in the bond markets seem primarily to entail interest rate penalties both for issuers in the Pacific Northwest and issuers who are perceived to bear nuclear construction risks. Because there is no shared credit or backing of WPPSS bonds by Washington state, there should be little direct effect on Washington general obligation bonds from the WPPSS problems. Comparing the Bond Buyer Index (BBI, an index of average US bond yields) for five separate Washington state issues over the past three years provides a measure of the expected yield of a hypothetical average-quality general obligation issue during a given week. The Washington state issues did fairly well when measured against the BBI before the WPPSS problems, but began to pay a significant penalty as WPPSS

encountered difficulties. As noted, the state issue of \$150 million in August 1983 paid nearly a full percentage point penalty from its previous performance against the BBI—which has largely been seen as a WPPSS-related penalty required by investors.

This penalty — millions of dollars over the life of the bonds — may prove to be simply the region's first instalment of indirect payment for the WPPSS default. Since then, however, the state bonds have fared somewhat better: as early as 26 October 1983 interest rates for Washington state issues were relatively lower, indicating that the WPPSS penalty was already beginning to fade. Nevertheless, the downgrading of the Snohomish Public Utility District No. 1 bonds and the Baa rating for its \$242 million hydroelectric revenue bond issue in November 1983 are examples of a regional WPPSS penalty as well as an indication of its effects on the public power entities involved.

Further evidence of the impact of WPPSS is provided by the secondary market trading for public power issues. When WPPSS projects 4 and 5 approached default, not all public power issues were affected uniformly. Only those with considerable nuclear construction exposure and a history of project delays, cost increases and strong reliance on take-or-pay contracts suffered substantial penalties.

These effects were evident on bonds for the Massachusetts Municipal Wholesale Electric Company and the North Carolina Municipal Power Agency No. 1, despite the many differences between these undertakings and WPPSS. Issuers with fewer perceived similarities to WPPSS, such as the Municipal Electric Authority of Georgia, suffered relatively little¹⁹.

The market's reception of the first two joint-action public power issues in the wake of the WPPSS default is also significant. Both the MPPA bonds on 14 September and the \$211 million Southern Minnesota Municipal Power Agency issue on 29 September went to construction coal-fired power plants under construction by investor-owned utilities. The MPPA issue, rated A1/A+, and the Southern Minnesota issue, rated A/A–, sold at yields of 10.7 per cent and 10.05 per cent, respectively, at the longest maturity. Contrary to some expectations, both sales proceeded smoothly.

One financial analyst has stated that the decision by the Washington State Court created serious problems for investors in municipal utility bonds (issued by a city to construct power facilities), the sanctity of which has rarely been questioned. It had been assumed that the municipal utility's ratepayers would bear any risks associated with terminated projects. This analyst concluded that the court's decision implies that the bond-holders rather than the ratepayers can now expect to be at risk if a project fails.

This may, however, be an overreaction,

for the court decision was based strictly on Washington state law. Whether municipal utilities in other states have authority to enter into take-or-pay contracts depends upon their own state laws, which vary widely. If it is in fact true that the \$150 million sale by Washington state carried an interest premium of 75–100 basis points because of the WPPSS default, and if the Michigan sale carried an interest premium (but of smaller magnitude) for the same reason, then it appears that the effects of the WPPSS default are lessening.

Nevertheless, it is difficult to believe that the large yield spread does not reflect some interest premium associated with the WPPSS default. The issue is further clouded by the fact that, in recent years, individuals have purchased about 75 per cent of new municipal bond issues, whereas commercial banks and insurance companies were previously much larger participants¹². Attracting individual investors may in the future require a margin of 25–50 basis points, and while a difference of 0.003 or 0.004 in price may seem trivial, when viewed across an \$80,000 million bond market this implies additional annual financing costs in excess of \$400 million. Some analysts consider that the WPPSS default has had an effect on interest rates and note that, over the past year, the interest differentials for Washington state and local government issues have been about one per cent.

Three major conclusions seem to emerge. First, the impact of the WPPSS default in both the municipal bond market as a whole and the public power market in particular has been substantial, but less than feared. Second, investors are differentiating among public power issues and are discriminating against particular issues that resemble WPPSS. Third, it may be too soon to speculate on the long-run impact of WPPSS: the first missed semiannual interest payments on bonds for plants 4 and 5 were only in January 1984; it will be years before the myriad legal issues are resolved and the markets will be greatly affected by the ultimate fate of other troubled nuclear power projects.

Whose fault?

In surveying the events that led to the WPPSS default, it is tempting to single out a particular villain or set of villains, and there is no shortage of blame to be dispensed. In retrospect, it is obvious that the energy demand forecasts relied upon in the decisions to construct the WPPSS nuclear power plants were wrong in forecasting regional energy shortages for the 1980s based on the experiences of the 1960s and early 1970s. But with the present oil glut, it is easy to forget the mood of panic and doom concerning the world's energy future which followed the 1973 oil embargo and subsequent oil price increases. Studies and analyses of the "energy crisis" over the past decade show that the overwhelming weight of expert opinion was

that the world had entered a new era of scarce and expensive energy, for which demand was almost unlimited^{20,21}.

In the light of the problems of the nuclear power industry in recent years, the original cost estimates of the WPPSS nuclear power plants appear unrealistically low and the four-five-and-six-fold increase of construction costs are not at all surprising. However, when the construction decisions were made in the early 1970s, not only did the United States seem to be confronting a permanent energy crisis, but nuclear power appeared to be an inexpensive and almost inexhaustible power source. For two decades nuclear power was advertised as being "too cheap to meter" and many of the nuclear power plants constructed during the 1960s were producing reliable, inexpensive electricity and seemed to be fulfilling the promise (see Ch. 5, ref. 22). Who, more than a decade ago, accurately predicted the problems that have plagued the nuclear power industry in recent years, especially since the accident at Three Mile Island? In seriously misjudging the costs of and requirement for nuclear power, the WPPSS decision-makers enjoy much distinguished company.

Criticisms can be made of other aspects of the WPPSS fiasco. The administrators and financial managers were clearly unequal to the task, while the free access which WPPSS enjoyed to the capital markets throughout the 1970s did little to enforce prudent financial discipline. The underwriters of the WPPSS bonds, the major Wall Street investment firms, have come in for some well-deserved criticism, and the Securities and Exchange Commission has undertaken a wide-ranging investigation of the handling by the brokerage houses of the sale of the WPPSS bonds²³. Further, serious legal and ethical questions have been raised concerning the decision by the elected judges of the Washington State Supreme Court absolving the Washington utilities of their contractual obligations.

Terminated nuclear power plants are not uncommon throughout the country, yet none of the others have led to massive bond defaults. The WPPSS bond default occurred because those who promised to pay debt service on the bonds chose not to pay, and convinced the highest court of the State of Washington to clothe their unwillingness to pay with a cloak of legal authority. Those two factors—the participants' unwillingness to pay and the Washington Supreme Court's acquiescence in that unwillingness—are what make WPPSS a "debacle". The real lesson is that security for debt resting on state law is no stronger than the integrity of those who make and interpret state law.

Rather than apportioning blame, it is more fruitful to consider what benefits may eventually emerge from the debacle. At base, what "Whoops" represents is a breakdown in accountability between

politicians, administrators and private investment firms. It illustrates what can happen when independent off-budget enterprises, which are often unaccountable but which are empowered to issue tax-exempt securities, interact with profit-seeking underwriters and bond-rating agencies. WPPSS may be the tip of the iceberg: in recent years, off-budget financing has expanded rapidly as state and local governments have sought to avoid the ire of taxpayers as well as mandated spending limitations. The off-budget state and local public sector now rivals the on-budget sector — nearly three-quarters of state and local borrowing is off-budget²⁴.

At the least, then, two benefits may emerge. First, the actions and good judgments of the bond-rating agencies and underwriters, upon which the investing public must rely, have been found to be seriously in question. The negative publicity, bond-holder suits and government investigations provided by WPPSS may generate necessary improvements in rating agencies and underwriters. Second, perhaps WPPSS will result in a long overdue re-examination by Congress and state governments of the bewildering array of quasi-government agencies, rapidly proliferating, which benefit from tax-exempt or preferential interest rates and debt financing arrangements. □

Roger H. Bezdek is in the US Department of the Treasury, Office of the Secretary, Washington, DC 20220, USA. The views expressed here are those of the author and do not reflect the views of the US Department of the Treasury.

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Computational vision and regularization theory

Tomaso Poggio, Vincent Torre* & Christof Koch

Artificial Intelligence Laboratory and Center for Biological Information Processing, Massachusetts Institute of Technology, 545 Technology Square, Cambridge, Massachusetts 02139, USA

* Istituto di Fisica, Università di Genova, Genova, Italy

Descriptions of physical properties of visible surfaces, such as their distance and the presence of edges, must be recovered from the primary image data. Computational vision aims to understand how such descriptions can be obtained from inherently ambiguous and noisy data. A recent development in this field sees early vision as a set of ill-posed problems, which can be solved by the use of regularization methods. These lead to algorithms and parallel analog circuits that can solve 'ill-posed problems' and which are suggestive of neural equivalents in the brain.

COMPUTATIONAL vision denotes a new field in artificial intelligence, centred on theoretical studies of visual information processing. Its two main goals are to develop image understanding systems, which automatically construct scene descriptions from image input data, and to understand human vision.

Early vision is the set of visual modules that aim to extract the physical properties of the surfaces around the viewer, that is, distance, surface orientation and material properties (reflectance, colour, texture). Much current research has analysed processes in early vision because the inputs and the goals of the computation can be well characterized at this stage (see refs 1-4 for reviews). Several problems have been solved and several specific algorithms have been successfully developed. Examples are stereomatching, the computation of the optical flow, structure from motion, shape from shading and surface reconstruction.

A new theoretical development has now emerged that unifies much of these results within a single framework. The approach has its roots in the recognition of a common structure of early vision problems. Problems in early vision are 'ill-posed', requiring specific algorithms and parallel hardware. Here we introduce a specific regularization approach, and discuss its implications for computer vision and parallel computer architectures, including parallel hardware that could be used by biological visual systems.

Early vision processes

Early vision consists of a set of processes that recover physical properties of the visible three-dimensional surfaces from the two-dimensional intensity arrays. Their combined output roughly corresponds to Marr's 2-1/2D sketch¹, and to Barrow and Tennenbaum's intrinsic images⁵. Recently, it has been customary to assume that these early vision processes are general and do not require domain-dependent knowledge, but only

generic constraints about the physical world and the imaging stage (see box). They represent conceptually independent modules that can be studied, to a first approximation, in isolation. Information from the different processes, however, has to be combined. Furthermore, different modules may interact early on. Finally, the processing cannot be purely 'bottom-up': specific knowledge may trickle down to the point of influencing some of the very first steps in visual information processing.

Computational theories of early vision modules typically deal with the dual issues of representation and process. They must specify the form of the input and the desired output (the representation) and provide the algorithms that transform one into the other (the process). Here we focus on the issue of processes and algorithms for which we describe the unifying theoretical framework of regularization theories. We do not consider the equally important problem of the primitive tokens that represent the input of each specific process.

A good definition of early vision is that it is inverse optics. In classical optics or in computer graphics the basic problem is to determine the images of three-dimensional objects, whereas vision is confronted with the inverse problem of recovering surfaces from images. As so much information is lost during the imaging process that projects the three-dimensional world into the two-dimensional images, vision must often rely on natural constraints, that is, assumptions about the physical world, to derive unambiguous output. The identification and use of such constraints is a recurring theme in the analysis of specific vision problems.

Two important problems in early vision are the computation of motion and the detection of sharp changes in image intensity (for detecting physical edges). They illustrate well the difficulty of the problems of early vision. The computation of the two-dimensional field of velocities in the image is a critical step in several schemes for recovering the motion and the three-dimensional structure of objects. Consider the problem of determining the velocity vector V at each point along a smooth contour in the image. Following Marr and Ullman⁶, one can assume that the contour corresponds to locations of significant intensity change. Figure 1 shows how the local velocity vector is decomposed into a normal and a tangential component to the curve. Local motion measurements provide only the normal component of velocity. The tangential component remains 'invisible' to purely local measurements (unless they refer to some discontinuous features of the contour such as a corner). The problem of estimating the full velocity field is thus, in general, underdetermined by the measurements that are directly available from the image. The measurement of the optical flow is inherently ambiguous. It can be made unique only by adding information or assumptions.

The difficulties of the problem of edge detection are somewhat different. Edge detection denotes the process of identifying the

Examples of early vision processes

- Edge detection
- Spatio-temporal interpolation and approximation
- Computation of optical flow
- Computation of lightness and albedo
- Shape from contours
- Shape from texture
- Shape from shading
- Binocular stereo matching
- Structure from motion
- Structure from stereo
- Surface reconstruction
- Computation of surface colour

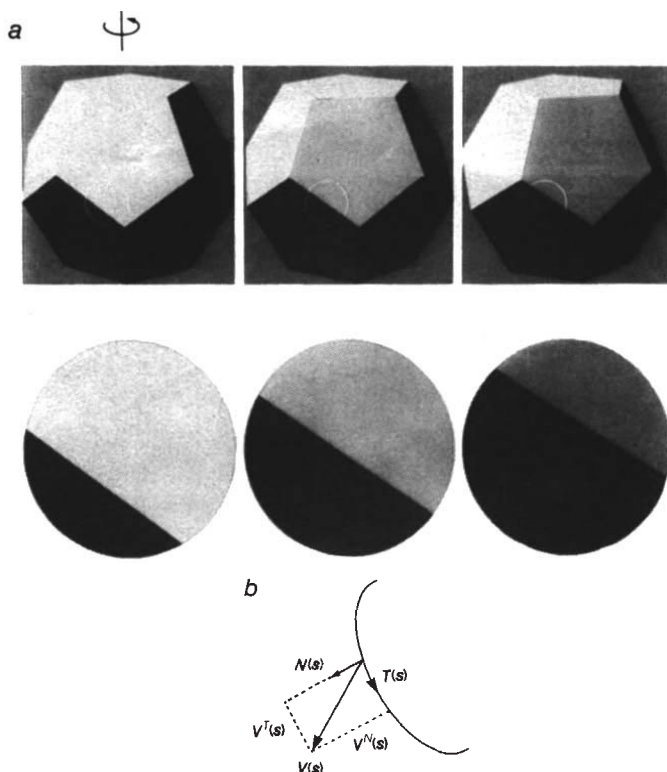


Fig. 1 Ambiguity of the velocity field. *a*, Local measurements cannot measure the full velocity field in the image plane, originated here by three-dimensional rotation of a solid object (three frames are shown). Any process operating within the aperture (shown as a white circle) can compute only the component of motion perpendicular to the contour. *b*, Decomposition of the velocity vector along the contour, parametrized by the arc length s into components normal ($V^N(s)$) and tangential ($V^T(s)$) to the curve. The computer drawing was kindly provided by Karl Sims.

physical boundaries of three-dimensional surfaces from intensity changes in their image. What is usually intended with edge detection is a first step towards this goal, that is, detecting and localizing sharp changes in image intensity. This is a problem of numerical differentiation of image data, which is plagued by the noise unavoidable during the imaging and the sampling processes. Differentiation amplifies noise and this process is thus inherently unstable. Figure 3 shows an example of an edge profile and its second derivative, where noise is significantly amplified. Most problems in early vision present similar difficulties. They are mostly underconstrained, as in the computation of the optical flow, or not robust against noise, as in edge detection.

Ill-posed problems

The common characteristics of most early vision problems (in a sense, their deep structure) can be formalized: most early vision problems are ill-posed problems in the precise sense defined by Hadamard^{7,8}. This claim captures the importance of constraints and reflects the definition of vision as inverse optics.

Hadamard first introduced the definition of ill-posedness in the field of partial differential equations⁹. Although ill-posed problems have been considered for many years as almost exclusively mathematical curiosities, it is now clear that many ill-posed problems, typically inverse problems, are of great practical interest (for instance, computer tomography). A problem is well-posed when its solution exists, is unique and depends continuously on the initial data. Ill-posed problems fail to satisfy one or more of these criteria. Note that the third condition does not imply that the solution is robust against noise in practice. For this, the problem must not only be well-posed but also be well conditioned to ensure numerical stability¹⁰.

It is easy to show formally that several problems in early vision are ill-posed in the sense of Hadamard⁸: stereo matching, structure from motion, computation of the optical flow, edge detection, shape from shading, the computation of lightness and surface reconstruction. Computation of the optical flow is ill-posed because the 'inverse' problem of recovering the full velocity field from its normal component along a contour fails to satisfy the uniqueness condition. Edge detection, intended as numerical differentiation, is ill-posed because the solution does not depend continuously on the data.

The main idea for 'solving' ill-posed problems, that is for restoring 'well-posedness', is to restrict the class of admissible solutions by introducing suitable *a priori* knowledge. *A priori* knowledge can be exploited, for example, under the form of either variational principles that impose constraints on the possible solutions or as statistical properties of the solution space. We will use the general term regularization for any method used to make an ill-posed problem well-posed. Variational regularization will indicate the regularization methods that reformulate an ill-posed problem in terms of a variational principle. We will next outline specific variational methods that we will denote as the standard regularization methods, attributable mainly to Tikhonov^{11,12} (see also refs 13, 14). We will also outline future extensions of the standard theory from the perspective of early vision.

The regularization of the ill-posed problem of finding z from the 'data' y

$$Az = y \quad (1)$$

requires the choice of norms $\|\cdot\|$ and of a stabilizing functional $\|Pz\|$. In standard regularization theory, A is a linear operator, the norms are quadratic and P is linear. Two methods that can be applied are^{8,13}: (1) among z that satisfy $\|Az - y\| \leq \epsilon$ find z that minimizes (ϵ depends on the estimated measurement errors and is zero if the data are noiseless)

$$\|Pz\|^2 \quad (2)$$

(2) find z that minimizes

$$\|Az - y\|^2 + \lambda \|Pz\|^2 \quad (3)$$

where λ is a so-called regularization parameter.

The first method computes the function z that is sufficiently close to the data and is most 'regular', that is minimizes the 'criterion' $\|Pz\|^2$. In the second method, λ controls the compromise between the degree of regularization of the solution and its closeness to the data. Standard regularization theory provides techniques for determining the best λ ^{12,15}. Thus, standard regularization methods impose the constraints on the problem by a variational principle, such as the cost functional of equation (3). The cost that is minimized reflects physical constraints about what represents a good solution: it has to be both close to the data and regular by making the quantity $\|Pz\|^2$ small. P embodies the physical constraints of the problem. It can be shown for quadratic variational principles that under mild conditions the solution space is convex and a unique solution exists. It must be pointed out that standard regularization methods have to be applied after a careful analysis of the ill-posed nature of the problem. The choice of the norm $\|\cdot\|$, of the stabilizing functional $\|Pz\|$ and of the functional spaces involved is dictated both by mathematical properties and by physical plausibility. They determine whether the precise conditions for a correct regularization hold for any specific case.

Variational principles are used widely in physics, economics and engineering. In physics, for instance, most of the basic laws have a compact formulation in terms of variational principles that require minimization of a suitable functional, such as the energy or the lagrangian.

Examples

Variational principles of the form of equation (3) have been used in the past in early vision¹⁶⁻²⁵. Other problems have now been approached in terms of standard regularization methods

Table 1 Regularization in early vision

Problem	Regularization principle
Edge detection	$\int [(Sf - i)^2 + \lambda (f_{xx})^2] dx$
Optical flow (area based)	$\int [i_x u + i_y v + i_z]^2 + \lambda (u_x^2 + u_y^2 + v_x^2 + v_y^2) dx dy$
Optical flow (contour based)	$\int [(V \cdot N - V^N)^2 + \lambda ((\partial/\partial s)V)^2] ds$
Surface reconstruction	$\int [S \cdot f - d]^2 + \lambda (f_{xx}^2 + 2f_{xy}^2 + f_{yy}^2) dx dy$
Spatiotemporal approximation	$\int [(S \cdot f - i)^2 + \lambda (\nabla f \cdot V + ft)^2] dx dy dt$
Colour	$\ I^v - Az\ ^2 + \lambda \ Pz\ ^2$
Shape from shading	$\int [(E - R(f, g))^2 + \lambda (f_x^2 + f_y^2 + g_x^2 + g_y^2)] dx dy$
Stereo	$\int \{[\nabla^2 G * (L(x, y) - R(x + d(x, y), y))]^2 + \lambda (\nabla d)^2\} dx dy$

Some of the early vision problems that have been solved in terms of variational principles. The first five are standard quadratic regularization principles. In edge detection^{26,27} the data on image intensity ($i = i(x)$) (for simplicity in one dimension) are given on a discrete lattice: the operator S is the sampling operator on the continuous distribution f to be recovered. A similar functional may be used to approximate time-varying imagery. The spatio-temporal intensity to be recovered from the data $i(x, y, t)$ is $f(x, y, t)$; the stabilizer imposes the constraint of constant velocity V in the image plane (ref. 61). In area-based optical flow¹⁸, i is the image intensity, u and v are the two components of the velocity field. In surface reconstruction^{21,22} the surface $f(x, y)$ is computed from sparse depth data $d(x, y)$. In the case of colour³² the brightness is measured on each of three appropriate colour coordinates I^v ($v = 1, 2, 3$). The solution vector z contains the illumination and the albedo components separately; it is mapped by A into the ideal data. Minimization of an appropriate stabilizer enforces the constraint of spatially smooth illumination and either constant or sharply varying albedo. For shape from shading¹⁹ and stereo (T.P. and A. Yuille, unpublished), we show two non-quadratic regularization functionals. R is the reflectance map, f and g are related to the components of the surface gradient, E is the brightness distribution¹⁹. The regularization of the disparity field d involves convolution with the laplacian of a gaussian of the left (L) and the right (R) images and a Tikhonov stabilizer corresponding to the disparity gradient.

(see Table 1). Most stabilizing functionals used so far in early vision are of the Tikhonov type, being linear combinations of the first p derivatives of the desired solution z (ref. 12). The solutions arising from these stabilizers correspond to either interpolating or approximating splines. We return now to our examples of motion and edge detection, and show how standard regularization techniques can be applied.

Intuitively, the set of measurements of the normal component of velocity over an extended contour should provide considerable constraint on the global motion of the contour. Some additional assumptions about the nature of the real world are needed, however, in order to combine local measurements at different locations. For instance, the assumption of rigid motion on the image plane is sufficient to determine V uniquely^{23,24}. In this case, local measurements of the normal component at different locations can be used directly to find the optical flow, which is the same everywhere. The assumption, however, is overly restrictive, because it does not cover the case of motion of a rigid object in three-dimensional space (see Fig. 1). Hildreth suggested^{23,24}, following Horn and Schunck¹⁸, a more general smoothness constraint on the velocity field. The underlying physical consideration is that the real world consists of solid objects with smooth surfaces, whose projected velocity field is usually smooth. The specific form of the stabilizer (a Tikhonov stabilizer) was dictated by mathematical considerations, especially uniqueness of the solution. The two regularizing methods correspond to the two algorithms proposed and implemented by Hildreth²³. The first one, which assumes that the

measurements of the normal velocity components $V^N(s)$ are exact, minimizes

$$\|PV\|^2 = \int \left(\frac{\partial V}{\partial s} \right)^2 ds \quad (4)$$

subject to the measurements of the normal component of velocity (where s is arc length). The integral is evaluated along the contour. For non-exact data the second method provides the solution by minimizing

$$\|V \cdot N - V^N\|^2 + \lambda \int \left(\frac{\partial V}{\partial s} \right)^2 ds \quad (5)$$

where N is the normal unit vector to the contour and λ^{-1} expresses the reliability of the data. Figure 2a shows an example of a successful computation of the optical flow by the first algorithm.

Recently, regularization techniques have been applied to edge detection^{26,27}. The problem of numerical differentiation can be regularized by the second method with a Tikhonov stabilizer that reflects a constraint of smoothness on the image (see Table 1). The physical justification is that the image is an analytical function with bounded derivatives, because of the band-limiting properties of the optics that cuts off high spatial frequencies. This regularized solution is equivalent, under mild conditions, to convolving the intensity data with the derivative of a filter similar to the gaussian²⁶ (see Fig. 3), proposed earlier^{28,29}.

Other early vision problems can be solved by standard regularization techniques. Surface reconstruction, for example, can be performed from a sparse set of depth values by imposing smoothness of the surface²⁰⁻²². Optical flow can be computed at each point in the image, rather than along a contour, using a constraint of smooth variation, in the form of a Tikhonov stabilizer¹⁷. Variational principles that are not exactly quadratic but have the form of equation (3) can be used for other problems in early vision. The main results of Tikhonov can in fact be extended to the case in which the operators A and P are nonlinear, provided they satisfy certain conditions³⁰. The variation of an object's brightness gives clues to its shape: the surface orientation can be computed from an intensity image in terms of the variational principle shown in Table 1, which penalizes orientations violating the smoothness constraint and the irradiance constraint¹⁸. Stereo matching is the problem of inferring the correct binocular disparity (and therefore depth) from a pair of binocular images, by finding which feature in one image corresponds to which feature in the other image. This is an ill-posed problem which, under some restrictive conditions corresponding to the absence of occlusions, can be regularized by a variational principle that contains a term measuring the discrepancy between the feature maps extracted from the two images and a stabilizer that penalizes large disparity gradients (see Table 1) and effectively imposes a disparity gradient limit. The algorithm can reduce to an area-based correlation algorithm of the Nishihara type³¹ if the disparity gradient is small. A standard regularization principle has been proposed for solving the problem of separating a material reflectance from a spatially varying illumination in colour images³². The algorithm addresses the problem known in visual psychophysics as colour constancy³³.

Physical plausibility and illusions

Physical plausibility of the solution, rather than its uniqueness, is the most important concern in regularization analysis. A physical analysis of the problem, and of its significant constraints, plays the main role⁸. The *a priori* assumptions required to solve ill-posed problems may be violated in specific instances where the regularized solution does not correspond to the physical solution. The algorithm suffers an optical illusion. A good example is provided by the computation of motion. The smoothness assumption of equation (5) gives correct results under some general conditions (for example, when objects have images consisting of connected straight lines³⁴). For some classes of motion and contours, the smoothness principle will not yield

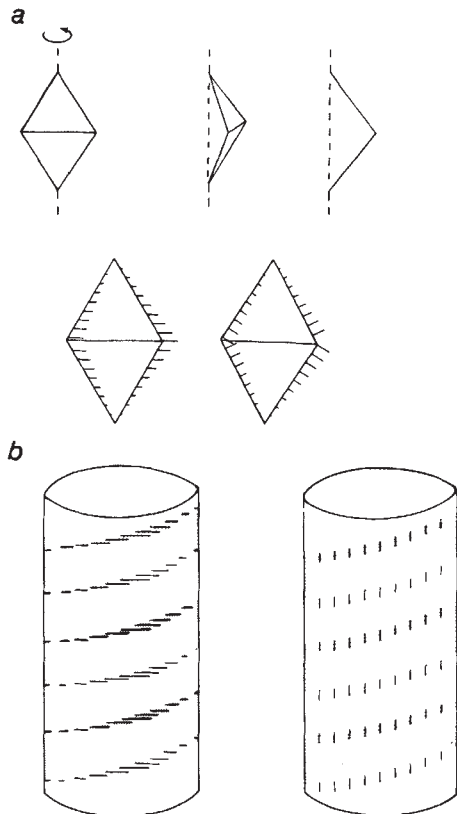


Fig. 2 Computing the smoothest velocity field along contours. *a*, Three-dimensional stimulus first used by Wallach⁶² to demonstrate the ability of the human visual system to derive three-dimensional structure from the projected two-dimensional motion of an object (kinetic depth effect). The top part shows three views of a figure as it is rotated around the vertical axis. The initial measurements of the normal velocity components V_i^N are shown on the lower right. The velocity field computed using equation (4) is shown on the lower left. The final solution corresponds to the physical correct velocity distribution. Recent electrophysiological evidence implicates the middle temporal area of the monkey as a site where a similar motion integration may occur⁶³. *b*, Circular helix on an imaginary three-dimensional cylinder, rotating about its vertical axis (barber pole). The projection of the curve onto the image plane, together with the resulting two-dimensional velocity vectors are drawn on the left. Although the true velocity field V is strictly horizontal (left), the smoothest velocity field (right) is vertical. This example illustrates a case where both the algorithm and the human visual system suffer the same optical illusion. Adapted from ref. 23.

the correct velocity field. In several of these cases, however, the human visual system also seems to derive a similar, incorrect velocity field, thereby possibly revealing *a priori* assumptions the brain is making about the world. A striking instance is the barber-pole illusion²³ (illustrated in Fig. 2*b*).

Analog networks

One of the mysteries of biological vision is its speed. Parallel processing has often been advocated as the answer to this problem. The model of computation provided by digital processes is, however, unsatisfactory, especially given the increasing evidence that neurones are complex devices, very different from simple digital switches. It is, therefore, interesting to consider whether the regularization approach to early vision may lead to a different type of parallel computation. We have recently suggested that linear, analog networks (either electrical or chemical) are, in fact, a natural way of solving the variational principles dictated by standard regularization theory⁷ (see also refs 22, 35).

The fundamental reason for such a mapping between variational principles and electrical or chemical networks is Hamilton's least action principle. The class of variational principles

that can be computed by analog networks is given by Kirchhoff's current and voltage laws, which represent conservation and continuity restrictions satisfied by each network component (appropriate variables are usually voltage and current for electrical networks and affinity and turnover rate for chemical systems³⁶; see also ref. 37). There is in general no unique network but possibly many networks implementing the same variational principle. For example, graded networks of the type proposed by Hopfield in the context of associative memory³⁸ can solve standard regularization principles³⁹.

From Kirchhoff's law, it can be proved⁷ that for every quadratic variational problem with a unique solution (which is usually the case⁸), there exists a corresponding electrical network consisting of resistances and voltage or current sources having the same solution. In other words, the steady-state current (or voltage) distribution in the network corresponds to the solution, for example to the tangential velocity distribution $V^T(s)$, of the standard regularization problem (Fig. 4). Furthermore, when capacitances are added to the system, thereby introducing dynamics, the system is stable. The data are supplied by injecting currents or by introducing batteries, that is by constant current or voltage sources⁷.

This analog parallel model of computation is especially interesting from the point of view of the present understanding of the biophysics of neurones, membranes and synapses. Increasing evidence shows that electrotonic potentials play a primary role in many neurones⁴⁰. Mechanisms as diverse as dendrodendritic synapses^{41,42}, gap junctions⁴³, neurotransmitters acting over different times and distances⁴⁴, voltage-dependent channels that can be modulated by neuropeptides⁴⁵ and interactions between synaptic conductance changes⁴⁶ provide neurones with various different circuit elements. Patches of neural membrane are equivalent to resistances, capacitances and phenomenological inductances⁴⁷. Synapses on dendritic spines mimic voltage sources, whereas synapses on thick dendrites or the soma act as current sources^{48,49}. Thus, single neurones or small networks of neurones could implement analog solutions of regularization principles. Hypothetical neuronal implementations of the analog circuits of Fig. 4 have been devised, involving only one or two separate dendrites⁷.

Beyond standard regularization theory

The new theoretical framework for early vision clearly shows the attractions and the limitations that are intrinsic to the standard Tikhonov form of regularization theory. The main problem is the degree of smoothness required for the unknown function that has to be recovered. For instance, in surface interpolation, the degree of smoothness corresponding to the so-called thin-plate splines smoothes depth discontinuities too much, and often leads to unrealistic results²⁰ (discontinuities may, however, be detected and then used in a second regularization step⁶⁶).

Standard regularization theory deals with linear problems and is based on quadratic stabilizers. It leads therefore to the minimization of quadratic functionals and to linear Euler-Lagrange equations. Non-quadratic functionals may be needed to enforce the correct physical constraints (Table 1 shows the non-quadratic case of shape-from-shading). Even in this case, methods of standard regularization theory can be used³⁰, but the solution space is no longer convex and many local minima can be found in the process of minimization.

A non-quadratic stabilizer has been proposed for the problem of preserving discontinuities in the reconstruction of surfaces from depth data⁵⁰. The stabilizer, in its basic form attributable to Geman and Geman⁵¹ (a similar principle but without a rigorous justification was proposed by Blake⁵²; see also the variational continuity control of Terzopoulos⁶⁷), embeds prior knowledge about the geometry of the discontinuities (the line process) and, in particular, that they are continuous and often straight contours. In standard regularization principles, the search space has only one local minimum to which suitable algorithms always converge. For non-quadratic functionals, the search space may be similar to a mountain range with many

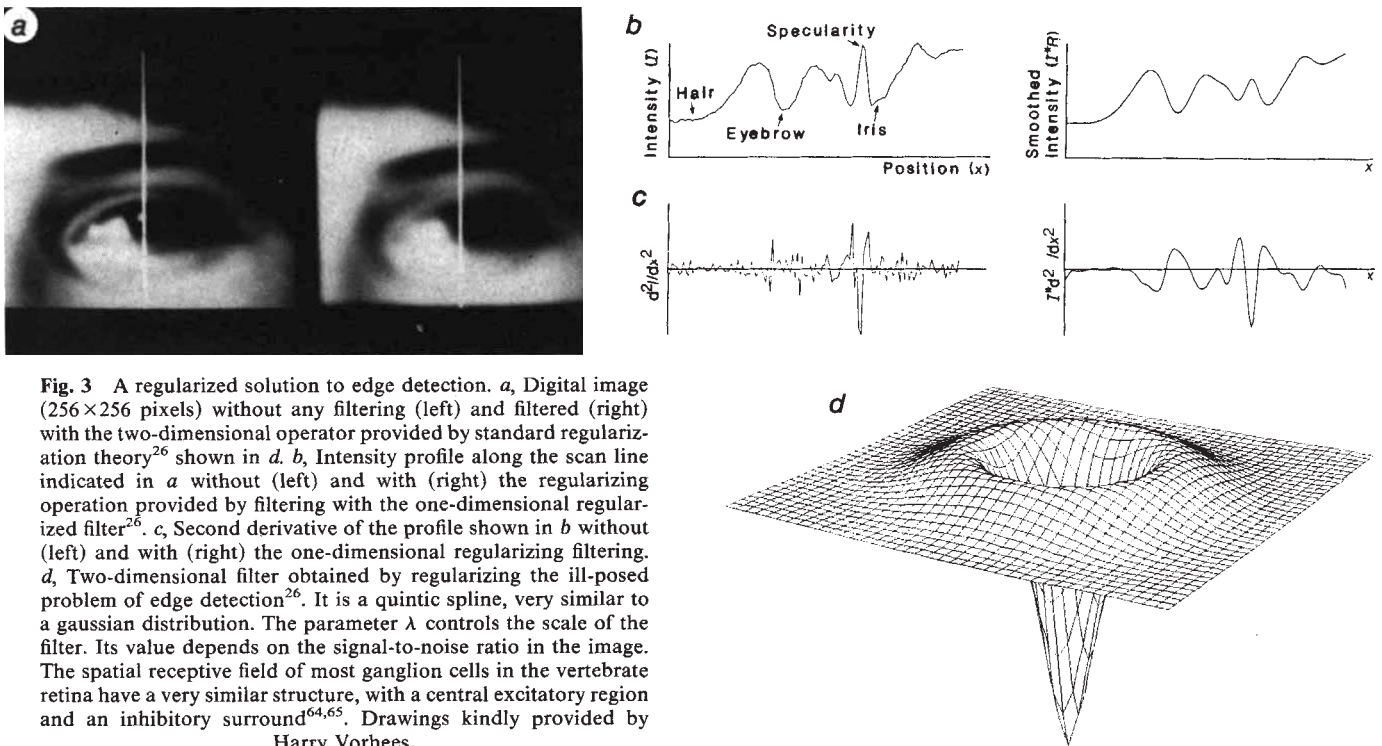


Fig. 3 A regularized solution to edge detection. *a*, Digital image (256×256 pixels) without any filtering (left) and filtered (right) with the two-dimensional operator provided by standard regularization theory²⁶ shown in *d*. *b*, Intensity profile along the scan line indicated in *a* without (left) and with (right) the regularizing operation provided by filtering with the one-dimensional regularized filter²⁶. *c*, Second derivative of the profile shown in *b* without (left) and with (right) the one-dimensional regularizing filtering. *d*, Two-dimensional filter obtained by regularizing the ill-posed problem of edge detection²⁶. It is a quintic spline, very similar to a gaussian distribution. The parameter λ controls the scale of the filter. Its value depends on the signal-to-noise ratio in the image. The spatial receptive field of most ganglion cells in the vertebrate retina have a very similar structure, with a central excitatory region and an inhibitory surround^{64,65}. Drawings kindly provided by Harry Vorhees.

local minima. Stochastic algorithms for solving minimization problems of this type have been proposed recently, to escape from local minima at which simple hill-climbing algorithms would be trapped^{53–55}. The basic idea is somewhat similar to adding a forcing noise term to the search algorithm. If the non-quadratic variational principle can be represented in a nonlinear analog network (as in ref. 39), an appropriate source of gaussian noise could drive the analog network. The dynamics of the system would then be described by a nonlinear stochastic differential equation, representing a diffusion process.

The challenge now for the regularization theory of vision is to extend it beyond standard regularization methods. The universe of computations that can be performed in terms of quadratic functionals is rather restricted. To see this, it is sufficient to realize that minimization of quadratic cost functionals leads to a linear regularization operator, that is, to a linear mapping of the input data into the solution space. In the special case when the data are on a regular grid and obey suitable conditions, the linear operator may become a convolution, that is, a simple filtering operation on the data. Similar to linear models in physics, standard regularization theory is an extremely useful approximation in many cases, but cannot deal with the full complexity of vision.

Stochastic route to regularization

A different rigorous approach to regularization is based on Bayes estimation and Markov random fields models. In this approach the *a priori* knowledge is represented in terms of appropriate probability distributions, whereas in standard regularization *a priori* knowledge leads to restrictions on the solution space. Consider as an example the case of surface reconstruction. A *priori* knowledge can be formulated in terms of a Markov random field (MRF) model of the surface. In a MRF the value at one discrete location depends only on the values within a given neighbourhood. In this approach the best surface maximizes some likelihood criterion such as the maximum *a posteriori* estimate or the *a posteriori* mean of the MRF. It has been pointed out⁵⁰ that the maximum *a posteriori* estimate of a MRF is equivalent to a variational principle of the general form of equation (3); the first term measures the discrepancy between the data and the solution, the second term is now an arbitrary potential function of the solution (defined on a discrete lattice). The overall variational principle, in general not quadratic,

reduces to a quadratic functional of the standard regularization type when the noise is additive and gaussian and first-order differences of the field are zero-mean, independent, gaussian random variables. In this case the maximum *a posteriori* estimate (MAP) coincides with all estimates and, in particular, with the *a posteriori* mean. But Marroquin⁵⁶ has shown recently that this is not true in general: in most cases the MAP estimate is not optimal with respect to natural error measures and better estimates such as the *a posteriori* mean can be found. In these cases the problem is not equivalent to finding the global minimum of an energy functional: simulated annealing is not needed, and a Metropolis-type algorithm⁵⁵ can be used instead.

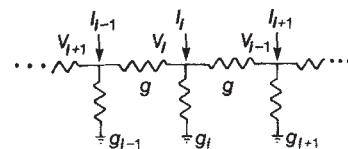


Fig. 4 Analog networks. A resistive network computing the smoothest velocity field²³. The network corresponds to the situation where the measurements of the normal velocity component V^N are assumed to be exact. Discretizing the associated variational equation (4) along the contour yields the Euler-Lagrange equations $(2 + \kappa_i^2) V_i^T - V_{i+1}^T - V_{i-1}^T = d_i$, where κ_i is the curvature of the contour at location i , d_i is a function of the data V_i^N and the contour and V_i^T is the unknown tangential component of the velocity V at location i along the contour. The equation describing the i th node in the electrical circuit is $(2g + g_i) V_i - g V_{i+1} - g_{i-1} V_{i-1} = I_i$, where V_i is the voltage corresponding to the unknown V_i^T , and I_i is the injected current at node i depending on the measurement V_i^N . A slightly more complicated circuit can be designed for the case when the measurements of V_i^N are not exact (equation (5)). Uniqueness of the regularized solution always ensures stability of the corresponding network, even if capacities are introduced. Equivalent analog networks can be implemented by diffusion-reaction systems, where the interaction between neighbouring locations are mimicked using diffusion or chemical reactions with first-order kinetics. Hypothetical neuronal implementations may be envisaged. The conductance g may correspond to a small segment of a dendrite, the variable conductance g_i to a synaptic input with a reversal potential close or equal to the resting potential of the dendrite (that is, silent or shunting inhibition) and the current source to a conventional chemical synapse injecting current I_i into the dendrite. The output is sampled at location i by a chemical synapse. Adapted from ref. 7.

In the case of Hildreth's motion computation²³ the smoothness assumption corresponds to the hypothesis that the changes in velocity between neighbouring points along the contour are zero-mean, independent, gaussian random variables. This connection between the stochastic approach and standard regularization methods gives an interesting perspective on the nature of the constraints and the choice of the stabilizer. The variational principles used to solve the inverse problems of vision correspond to the Markov structure that generates plausible solutions.

A related area of future investigation concerns the problem of learning a regularizing operator. In the case of standard regularization, the corresponding linear operator mapping the data into the solution may be learned by an associative learning scheme⁵⁷, of the type proposed in connection with biological memory⁵⁸.

Towards symbolic descriptions

So far, we have restricted our discussion to the early stages of vision that create image-like representations of the physical three-dimensional surfaces around the viewer. The step beyond these representations, also called intrinsic images⁵, or 2-1/2D sketches¹, is a large one. Intrinsic images are still image-like numerical representations, not yet described in terms of objects. They are already sufficient for some of the high-level tasks of a vision system such as manipulation and navigation. They cannot be used directly for the tasks of recognition and description that require the generation and use of more symbolic representations. It seems at first difficult to see how the computation of symbolic representations may fit at all in the perspective of regularizing ill-posed problems.

The basic idea of all regularization methods is to restrict the space of possible solutions. If this space is constrained to have finite dimensions, there is a good chance that an inverse problem will be well-posed. Thus, a representation based on a finite set of discrete symbols regularizes a possibly ill-posed problem. From this point of view, the problem of perception (regularizing an otherwise underconstrained problem using generic constraints of the physical world) becomes practically equivalent to the classical artificial intelligence problem of solving and inference, that is, of finding ways of solving intractable problems (such as chess) by limiting the search for solutions.

Conclusions

We suggest a classification of vision algorithms that maps naturally into parallel digital computer architectures now under development. Standard regularization, when sufficient, leads to two classes of parallel algorithms. Algorithms for finding minima of a convex functional such as steepest descent or the more efficient multigrid algorithms developed for vision⁵⁹ can always be used. They can be replaced by convolution algorithms if the data are given on a regular grid and A in equation (1) is space invariant. In the latter case, the regularized solution is obtained by convolving the data through a precomputed filter.

All these algorithms may be implemented by parallel architectures of many processors with only local connections. Problems that cannot be approached in terms of regularization and that require symbolic representations and operations on them, may need parallel architectures with a global communication facility, such as the Connection Machine currently under development⁶⁰.

The concept of ill-posed problems and the associated old and new regularization theories seem to provide a satisfactory theoretical framework for much of early vision. This new perspective also provides a link between the computational (ill-posed) nature of early vision problems, the structure of the algorithms for solving them and the parallel hardware that can be used for efficient visual information processing. It also shows the intrinsic limitations of the variational principles used so far in early vision, indicating at the same time how to extend regularization analysis beyond the standard theory.

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Microplate tectonics along a superfast seafloor spreading system near Easter Island

R. N. Hey*, D. F. Naar*, M. C. Kleinrock*, W. J. Phipps Morgan†, E. Morales‡ & J.-G. Schilling§

* Scripps Institution of Oceanography, La Jolla, California 92093, USA

† Brown University, Providence, Rhode Island 02912, USA

‡ Universidad Catolica de Valparaiso, Valparaiso, Chile

§ Graduate School of Oceanography, University of Rhode Island, Kingston, Rhode Island 02881, USA

There is a growing Easter microplate between the Pacific and Nazca plates. The eastern and western boundaries of the microplate are actively spreading and propagating north and south, respectively. The northern and southern boundaries are broad transform zones. Most of the interior of the microplate contains the sort of oblique sheared structures characteristic of zones of transferred lithosphere between propagating and failing spreading centres.

THE Easter microplate (Fig. 1) was first proposed to exist^{1,2} on the basis of the ring-shaped epicentral pattern, analysis of marine geophysical data and anomalous slip directions calculated from first-motion data. One hypothesis to explain the evolution of this area was that it is a stable growing microplate bounded by stable triple junctions³. Alternatively, the propagating rift hypothesis⁴⁻⁶ provided a possible explanation for this area in which an independent plate would exist only during the time necessary for the failing spreading centre completely to stop spreading as spreading on the propagating centre accelerates to the full Pacific-Nazca rate (see Fig. 10 of ref. 5).

Additional magnetic anomaly and bathymetric data were used to present the first detailed evolutionary interpretation of this area as resulting from rift propagation, and this analysis⁷ agrees with previous interpretations¹⁻³ that dual spreading centres are active. The most recent analysis was based on the seismicity distribution and newly determined earthquake mechanisms, as well as previously identified⁷ magnetic anomalies, and concluded that the region is best described as a rigid plate that is growing by rift propagation⁸.

During April 1983, we conducted a Sea Beam/magnetics survey of this large area of anomalous sea floor using the R/V

Thomas Washington. Our new data corroborate the existence, at least temporarily, of a microplate between two actively spreading segments of the East Pacific Rise (EPR), the East rift and West rift, which are propagating in opposite directions. However, the present tectonic configuration and recent tectonic evolution of this area differ in several important ways from previous interpretations. In particular, the best recent magnetic anomaly interpretation⁷ does not fit our new data on the East rift⁹ and the best recent tectonic model⁸ must therefore be altered.

Microplate boundaries

Eastern boundary. Figure 2 shows our new magnetic anomaly data combined with pre-existing data that we used to help define the present spreading centre configuration. The axial (Brunhes) anomaly is clearly defined over the southern part of the East rift. South of $\sim 26^{\circ}30'$ S, the Jaramillo event also appears to be present, and the Emperor reversed event¹⁰ at ~ 0.50 Myr BP is clearly evident between 26° S and 27° S, where the magnetic axis coincides with a narrow axial volcanic ridge (Figs 2, 3), indicating a spreading rate of ~ 120 mm yr⁻¹ (Fig. 3b). This rate is considerably slower than the 170–180 mm yr⁻¹ predicted here

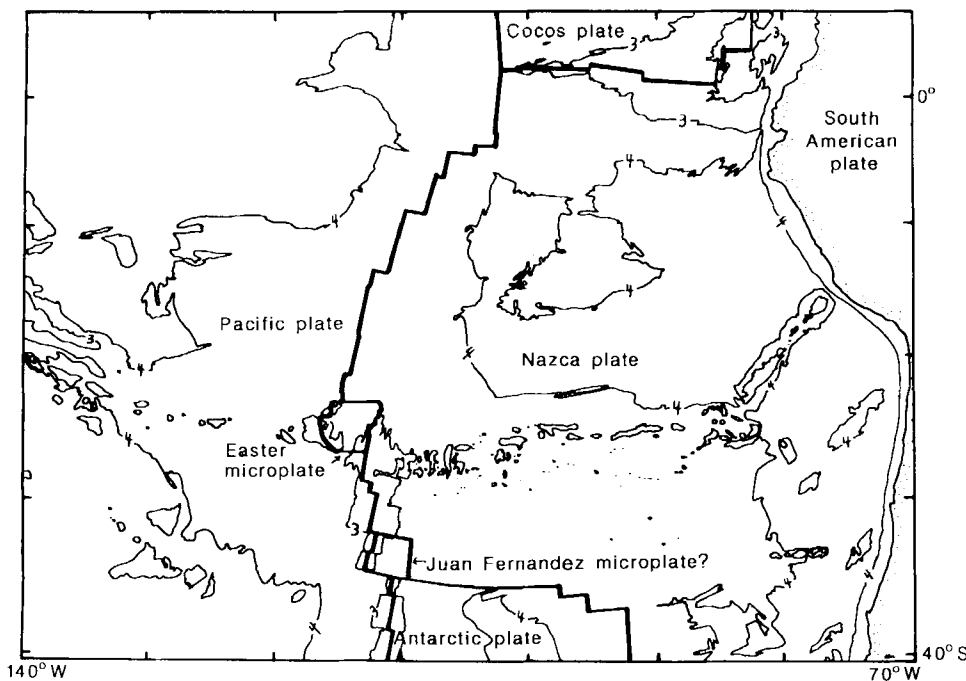
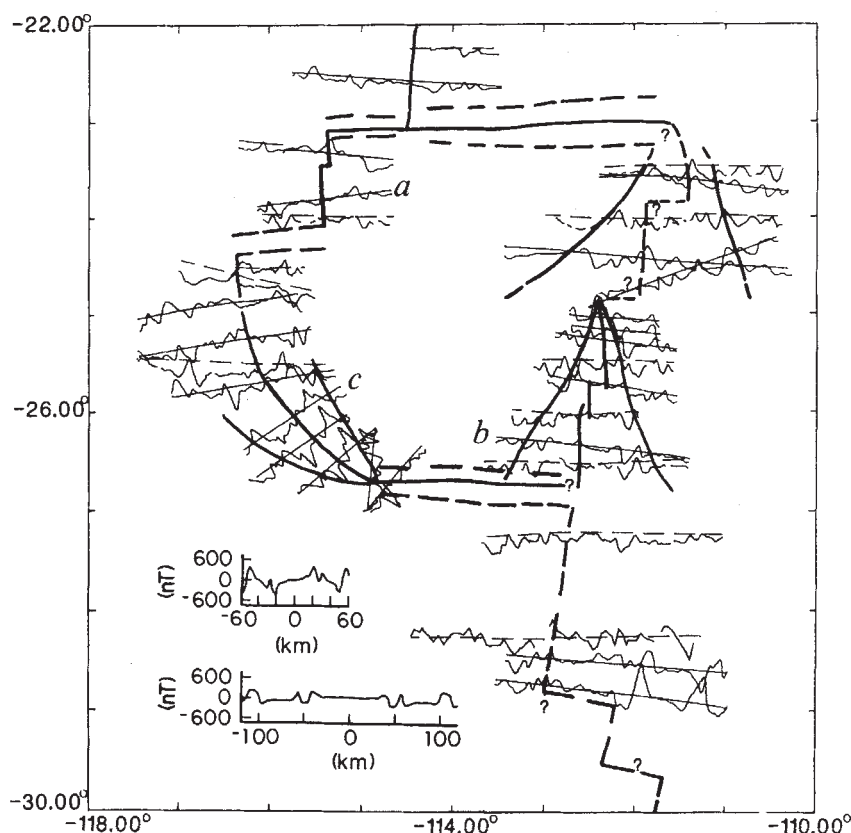


Fig. 1 Location map. Heavy lines, spreading centres; lighter connecting lines, transform faults. The 3- and 4-km isobaths are from ref. 48.

Fig. 2 Magnetic anomaly profiles plotted perpendicular to ship track. Solid tracklines, our new data; dashed tracklines, old data. Positive anomalies are above the trackline. Heavy lines, spreading centres and schematic transform boundaries, dashed where uncertain; V-shaped boundaries, pseudo-faults. The magnetic scale is the same as shown in two representative magnetic models (insets). The top model is generated assuming a spreading centre oriented 140° and spreading rate of 60 km Myr^{-1} . Note how the skewness of the top model matches the data on the South-west rift. The bottom model assumes a north-south ridge orientation and a spreading rate of 120 km Myr^{-1} . *a-c*, Profiles modelled in Fig. 3. Data from Scripps Geological Data Center.



for the Pacific–Nazca separation rate^{11–13}, and there is an indication that spreading rates are asymmetrical⁹.

One of the most conspicuous patterns in Fig. 2 is the northward narrowing of the Brunhes anomaly along this spreading centre to an apex just north of 25°S . This narrowing could result from rift propagation and/or slower spreading, although if it resulted solely from slower spreading it would indicate a rotation pole near 25°S with compression to the north. Detailed analysis of the magnetic anomalies and bathymetry⁹ indicates that the anomaly narrowing is best explained by a rift presently propagating to the north at a velocity of $\sim 150 \text{ km Myr}^{-1}$.

The geochemical pattern also supports the propagating rift interpretation, showing the characteristic^{14,15} increase in Fe and Ti content of basalts toward the propagator tip¹⁶. The bathymetric axis is 2,100 m high near $26^\circ 30' \text{S}$, where La/Sm in basalts also peaks¹⁶ and where some of the highest $^3\text{He}/^4\text{He}$ and $^{87}\text{Sr}/^{86}\text{Sr}$ isotope ratios occur^{17,18}, indicating that this marks either the hotspot location or the intersection of channelled flow from a hotspot¹⁹ to the rift^{16–18}. From there the axis deepens steadily to a 3,300-m-deep axial valley at the presumed propagator tip. This deep axis corresponds to a very narrow yet high-amplitude axial magnetic anomaly (Fig. 2). Similar patterns over the Galapagos 95.5°W propagator have been thought to result from anomalous magma cooling, crystal fractionation and viscous head loss as the rift breaks through old, cold lithosphere^{5,14,15}.

Our new Sea Beam vertical beam bathymetry, together with older bathymetry over the plate boundaries, are shown in Fig. 4. Sea Beam is a 12-kHz multi-narrow beam sonar system that generates nearly real-time contour images of swathes of sea floor. The contours are based on 16 cross-track depths computed each ping cycle, and the maximum contour swathe width is 73% of water depth^{20,21}. The power of this tool for marine tectonic studies is that the structural fabric of the sea floor is usually clearly delineated by a single swathe. A lineation map derived from our Sea Beam contours is shown in Fig. 5. The narrowing of the Brunhes anomaly corresponds to a V-shaped pattern of bathymetric lineaments which we interpret as pseudofaults⁶

bounding the lithosphere created on the propagating rift. Within this characteristic V-shaped propagator wake most lineations are north-south, parallel to the axis (exceptions suggest younger rift propagation). East of the eastern pseudofault the abyssal hill trends are similar to those created on the propagating rift, whereas west of the western pseudofault the seafloor fabric trends north-east to south-west, clearly oblique to the spreading axis. This is the type of pattern predicted by the continuous model of oceanic rift propagation^{5,22}, and observed over the Galapagos 95.5°W propagating rift system with Sea Beam, Deep-Tow and GLORIA^{23,24}.

There is no clearly defined axial anomaly denoting an active spreading boundary between the propagator tip near $24^\circ 50' \text{S}$ and the northern boundary of the microplate near 23°S . The tentative axial location shown is based on preliminary magnetic anomaly analysis, the epicentre pattern (Fig. 6), dredged fresh glasses¹⁶ and a zone of rough bathymetry narrowing to the north previously identified as formed at a propagating rift⁷, an interpretation corroborated by the extension of oblique structures north of the fast propagator tip (Fig. 5). The lack of a well-developed axial anomaly could mean that diffuse seafloor spreading is occurring or that there are multiple propagators creating chaotic magnetics in this area, which is bounded to the north by a broad east-west trending transform-like zone.

Northern boundary. The northern transform zone is well defined at 23°S , $114^\circ 30' \text{W}$ where it truncates the EPR segment to the north (Fig. 5) at what appears to be, at least instantaneously, the Pacific–Nazca–Easter rift–fracture–fracture (RFF) triple junction. This triple junction is essentially stable²⁵ because the Pacific–Easter and Easter–Nazca transforms are essentially colinear. South of the EPR terminus there is a shallow ($< 2,400 \text{ m}$) ridge extending west, and a deep ($> 3,700 \text{ m}$) trough extending east (Fig. 4). To the east, this Nazca–Easter boundary consists of en echelon east-west and ENE–WSW segments connected by oblique structures (Figs 4, 5). The overall trend of this zone near the triple junction is $\sim \text{N}85\text{E}$. There is a 5,300-m-deep hole near the eastern limit of the strong east-west structures, which may mark the intersection of this transform zone with the north-

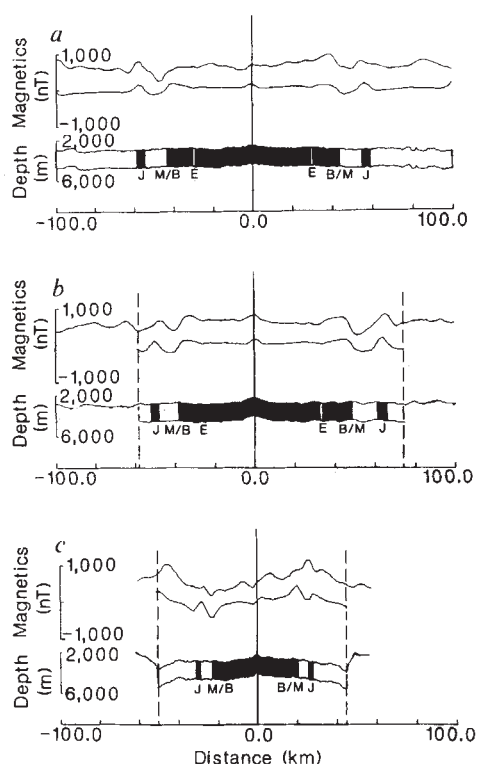


Fig. 3 Comparison of magnetic models with profiles indexed in Fig. 2. Top profile in each set, magnetic anomaly data; middle profile, model; lower profile, bathymetry, with magnetic source structure (darkened blocks are normal polarity). B, Brunhes anomaly; E, Emperor event; J, Jaramillo anomaly; M, Matuyama anomaly. Vertical dashed lines, postulated age of initiation of spreading (pseudo-faults) at these locations. The models are generated using the bathymetry and include a period of double magnetization intensity from 0.03 Myr BP to the present. Model *a* and *b* spreading rate is 120 km Myr⁻¹; model *b* is spreading 12% asymmetrically, faster to the east, starting at 1.1 Myr BP; model *c* spreading rate is 60 km Myr⁻¹ with 6% asymmetry, faster to the west, starting at 1.6 Myr BP. Spreading axis orientation is 0° for *a*, 5° for *b* and 140° for *c*.

eastern spreading axis. What part of this broad zone is active and what part represents previous activity is still uncertain. If the northeastern propagator is still propagating north, it is breaking through ~3-Myr-old lithosphere across an offset of ~300 km. These enormous scales could explain the great width and complexity of the northern boundary.

There is a puzzling group of earthquakes north of the microplate (Fig. 6) which includes north-west to south-east dextral or north-east to south-west sinistral strike-slip faulting and a significant NNE-SSW thrusting component⁸. West of these events there is a well-developed EPR axis seen clearly in our Sea Beam and magnetic anomaly data (which suggest asymmetrical accretion) and followed south to the triple junction using Sea Beam by P. J. Fox (personal communication). However, the spreading rate over this ridge is ≤ 140 mm yr⁻¹, which could mean there is another, as yet undiscovered, spreading axis to the east. At the junction the EPR axis curves towards the west (Fig. 5), indicating that the principal shear stress at the triple junction is the left-lateral shear along the Pacific-Easter transform, although the right-lateral Nazca-Easter transform is seismically more active. A component of compression along the northern microplate boundary (Fig. 6) may help to explain the seismicity pattern⁸.

West of the triple junction, the Pacific-Easter transform boundary trends nearly east-west (Fig. 5) to connect with the northernmost spreading segment of the West rift system. The Sea Beam lineations indicate that a fracture zone extends at the same azimuth 80 km farther west, suggesting that this geometry has been stable for at least 1 Myr.

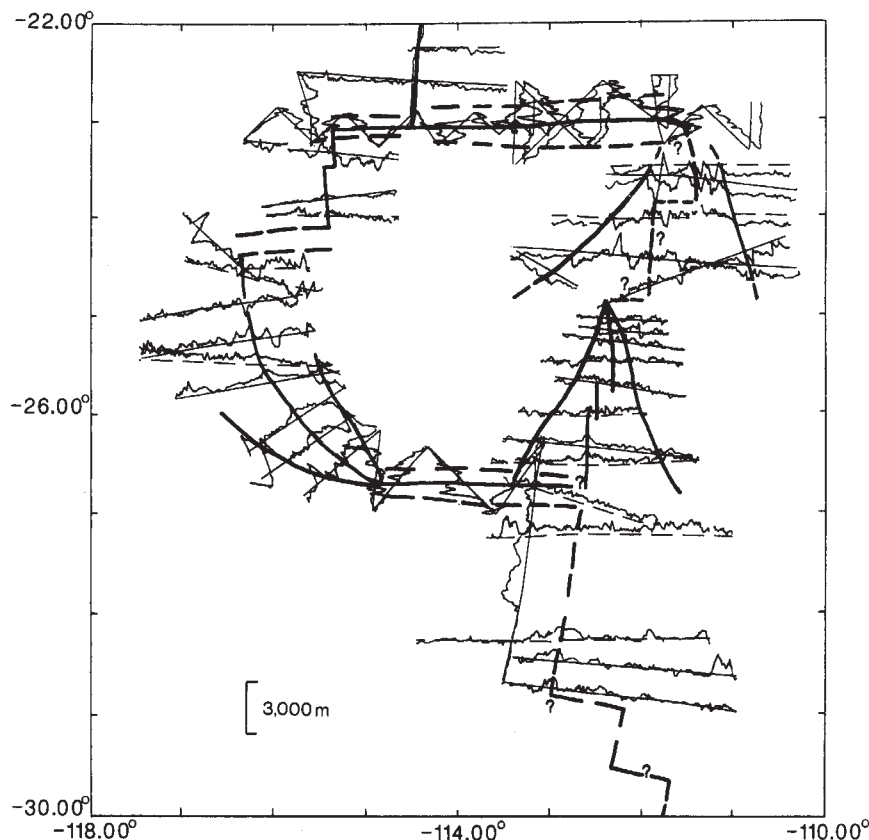
Western boundary. The western microplate boundary consists of three major spreading segments. Fresh glassy basalts dredged from each of these segments, together with those dredged on the eastern boundary, essentially confirm the existence of simultaneous spreading on the East and West rifts¹⁶. Our boundaries have been slightly modified based on the dredging results. The northern two segments trend roughly north-south (slightly west of north, Fig. 2) and are spreading at ~120–140 mm yr⁻¹ (Fig. 3a). These segments are offset by ~100 km along a sinistral transform zone near 24°15'S. The southwestern spreading segment trends north-west to south-east and appears to join the West rift at an axial kink near 25°30'S, or there may be a small transform-type offset which we are unable to resolve with our data.

The South-west rift is a clearly defined seafloor spreading system previously hypothesized^{3,7,8} but only now documented, which trends north-west to south-east (140°) in striking contrast to all other spreading segments in the area. It appears to be propagating towards the south-east. Two independent lines of evidence that demonstrate the north-west to south-east trend are the skewness of the magnetic anomalies, which can be well matched by the model anomalies if the spreading axis azimuth is ~140° (Fig. 3c), and the Sea Beam lineation orientations, which imply an azimuth of 120–145° (with some lineation fanning on opposite sides of the axis suggesting a nearby relative rotation pole, Fig. 5). The bathymetric axis (Fig. 4) has a more southerly trend than the bisector of the Brunhes/Matuyama reversal boundaries (Fig. 2), indicating asymmetrical and/or oblique spreading or very recent additional rift propagation with a more southerly azimuth. The bathymetry (Fig. 4) indicates an azimuth of 143° for the present spreading axis. The young crust created on this north-west to south-east oriented spreading centre is characterized by typical ridge-parallel bathymetric and magnetic patterns, bounded to the north-east and south-west by steep inward-facing scarps (Fig. 4). These scarps converge to the south and appear to be slightly diachronous, becoming older in the north (Figs 2, 4). Both scarps correlate well with major changes in Sea Beam lineations (Figs 4, 5). We therefore interpret these scarps as pseudofaults which indicate propagation to the south-east (at a rate of ~100 mm yr⁻¹). This interpretation is supported by the increase in Fe content of basalts toward the south-east¹⁶. Spreading rates appear to slow towards the south-east from ~90 to 50 mm yr⁻¹. Thus, both the eastern and western microplate boundaries are simultaneously active spreading centres, and the southern segments of these spreading systems are propagating in opposite directions.

Southern boundary. The South-west rift may curve south-east to merge with the southern transform boundary, or may be truncated by it, or there may be an en echelon ridge/transform geometry⁸. Although there is a suggestion (Figs 2, 4, 6) that one en echelon segment may exist, we have drawn an oversimplified east-west transform boundary where the focal mechanisms⁸ suggest east-west right-lateral strike-slip motion extending into what may be an RRF (rift-rift-fracture) or RFF triple junction. The spreading centres north and south of the junction seem to be co-linear but spreading at different rates, so asymmetrical spreading or ridge jumping may maintain the co-linearity, which could explain why the magnetic anomalies south of the microplate are so confused. This unstable RRF junction could evolve to a stable RFF configuration if the transforms were co-linear. If the southern transform boundary has evolved into a slow spreading centre⁸, it must be spreading very differently than the South-west rift. This boundary contains the shallowest and roughest bathymetry in the area as well as at the highest level of seismicity. We are only able to locate this boundary and the southern triple junction within a broad zone, and the seismicity pattern (Fig. 6) indicates additional complexities to the south.

Some of the shallow bathymetry may be seamounts derived from the mantle source presumably producing the anomalously shallow bathymetry of the microplate. These seamounts could show Pacific-hotspot motion, predicted to be 284° here¹¹, or

Fig. 4 Bathymetric profiles plotted perpendicular to the ship track, except for the northern and southern transform zones in which the data are projected east-west. Bathymetry shallower than 3,000 m is above trackline (or to the west for the transform zones). Tectonic elements and data sources are the same as in Fig. 2. Scale bar, 3,000 m.



could be leaking up along the southern boundary of the microplate.

There is no well-defined spreading axis south of this presumed southern boundary of the microplate until $\sim 31^\circ$ S (ref. 26; H. Craig, personal communication). The seismicity pattern (Fig. 6) suggests that there are two separate ~ 80 -km left-lateral transform offsets near 29° S and $29^\circ 30'$ S, which may be the fastest slipping transforms in the world.

Microplate interior

Most of the microplate interior is characterized by north-east to south-west seafloor fabric clearly oblique to the dominant north-south trend of the spreading centres and abyssal hill fabric surrounding the microplate (Fig. 5). Presumably, the microplate lithosphere was also created with this north-south fabric, but because of the time-progressive transferral of this lithosphere from one plate to another, the pre-existing fabric of the transferred lithosphere was sheared and tectonically rotated into the observed oblique trends characteristic of continuous rift propagation^{23,24}.

An earlier explanation^{7,8} for these oblique trends was that rotation of the microplate and East rift about a nearby relative rotation pole would produce 'fanned' lineations. However, the continuous rotation of abyssal hill fabric implied by this hypothesis is not seen in our Sea Beam data. There is little to no fanning on the Nazca plate (Fig. 5), and instead of continuous fanning on the microplate there are abrupt discontinuities (pseudofaults) separating lithosphere with quite different abyssal hill trends, indicating multiple episodes of rift propagation, perhaps six major episodes.

The pattern of spreading rates and epicentres suggests that at present the microplate is behaving as an independent plate rotating like a ballbearing between the Pacific and Nazca plates at a high angular velocity ($\sim 15^\circ$ per Myr clockwise) relative to the mantle about a pole located near the centre of the microplate. We emphasize that this interpretation is based on our preliminary analysis of spreading rates and plate motions. This analysis is complicated by the evident deformation of the micro-

plate (Fig. 5) and the complicated magnetic anomaly pattern, which makes some of the spreading rates suspect. To the extent that these rates are correct, the East and West rifts should be rotating rapidly clockwise, producing fanned anomalies on all the plates, but this is not observed (Fig. 5). One possible explanation is that the existing spreading centres, rather than being rotated to a new trend, are replaced by a series of propagators that each have roughly north-south azimuths. Thus, the spreading centre azimuth could essentially always be north-south and the anomalies rotated only on the microplate. Alternatively, oblique and asymmetrical spreading could produce the observed pattern. The hypothesized microplate rotation would produce complex patterns of compression and tension along the plate boundaries, as well as gradual propagation of the South-west rift along the southern transform boundary.

The scale of the microplate shearing is impressive (Fig. 5). Our Sea Beam data indicate that rift propagation has been generally continuous, with shear deformation distributed over the entire plate ($\sim 400 \times 400$ km), rather than episodic rift propagation with discrete transform faults and fracture zones (the degenerate form of pseudofaults), although some east-west structures could have resulted from pauses in propagation. The numerous intraplate earthquakes (Fig. 6) also indicate plate deformation.

Discussion

Here, we document the existence, at least temporarily, of an Easter microplate between two actively spreading segments of the EPR. We next speculate on the origin of the microplate and whether this is a transient or stable phenomenon. We prefer the explanation that it is a result of rift propagation on a very large scale and the existence of dual active spreading centres is a transient phenomenon arising because of the long time necessary for one spreading centre to slow and ultimately fail as the other gradually accelerates to take up all of the Pacific-Nazca separation. This large-scale rift propagation may be driven by gravitational stress produced by mantle convection^{5,27}.

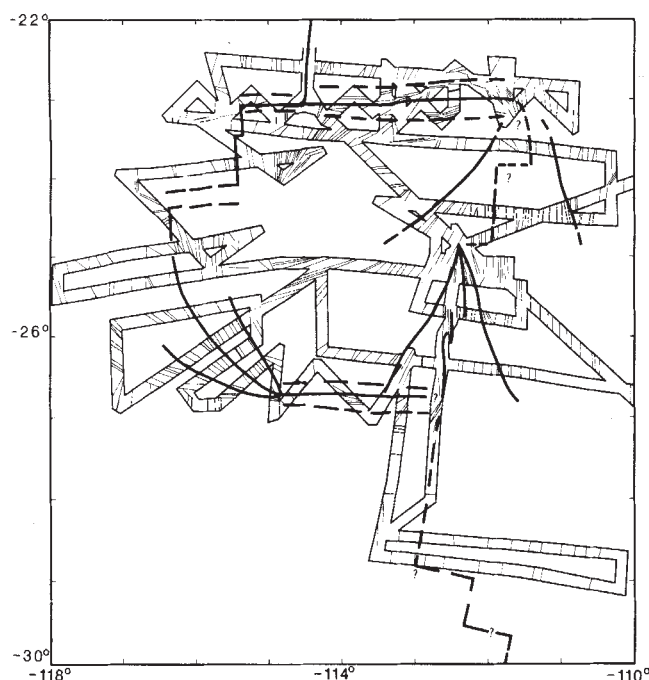


Fig. 5 Lination map generated from Sea Beam data. Lineations are extrapolated out to a swathe envelope which is four times the Sea Beam swathe width. Lineations subparallel to ship tracks are drawn as far as they are observed. Tectonic elements are the same as in Fig. 2.

Much evidence exists for unusually intensive mantle convection in this area, where present seafloor spreading rates are the fastest on Earth¹¹, and various hotspots, mantle plumes and mantle hot lines have been proposed under Easter Island, Sala y Gomez Island, south of the microplate, and near or under the East rift of the microplate near 27° S^{16-18,28-33} to explain the islands, seamounts and aseismic ridges extending away from this general area (Fig. 1). The microplate is near the centre of a huge region of anomalously shallow bathymetry³⁴, clearly delineated by the 4-km isobaths (Fig. 1), and correlates well with a broad region of anomalously low velocity surface waves as well as low shear wave velocities in the upper mantle³⁵. Further evidence for unusually extensive mantle convection in this area comes from the ³He/⁴He ratio in basalts dredged from the south-east boundary of the microplate, which is 11 times the atmospheric ratio, significantly greater than the mid-ocean ridge basalt values (8 ± 1 times atmospheric) found everywhere else along the EPR, which clearly shows the presence of a mantle plume component¹⁷. These results are consistent with an unusually warm and strongly convecting mantle and thin and weak lithosphere, which could be susceptible to non-rigid plate behaviour² or plate boundary reorganizations^{2,3,7,8,26}. Stresses produced by the intensive convection could perhaps cause the plate to break along more than one zone^{3,7}.

Dual spreading could also develop if the EPR segment closest to the hotspot tended to jump back toward the hotspot instead of migrating west with the rest of the EPR, a phenomenon previously proposed near the Iceland³⁶ and Galapagos³⁷ hotspots. All spreading centre jumps investigated in detail have resulted from rift propagation, and presumably all jumps involve propagation at some scale⁵. In order not to migrate off the hotspot, the East rift would need to spread at $\sim 120 \text{ mm yr}^{-1}$ (ref. 11), as observed⁹, and perhaps this helps to explain why the South-west rift, instead of failing, is still spreading at $\sim 60 \text{ mm yr}^{-1}$.

Dual spreading centres could also develop if there is a 'speed limit' for seafloor spreading centres³. The microplate is located along the fastest spreading ($\sim 170 \text{ mm yr}^{-1}$; ref. 26) part of the fastest active seafloor spreading system¹¹⁻¹³. Note that³ in wax modelling experiments³⁸ an 'island' sometimes temporarily

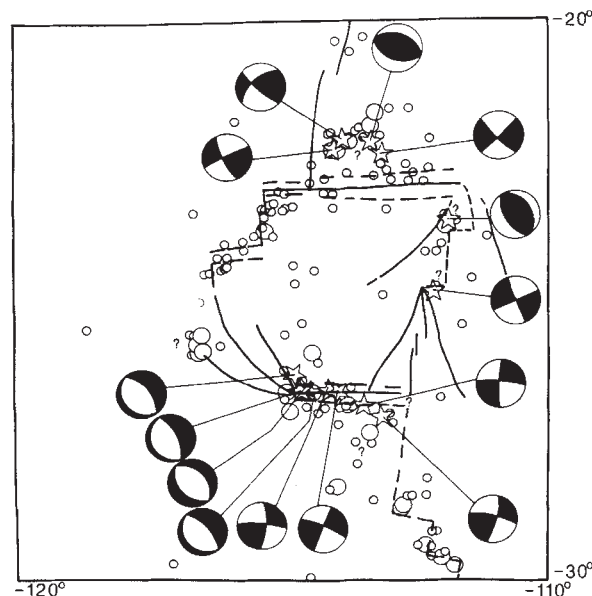


Fig. 6 Seismicity and focal mechanisms⁸ and our tectonic interpretation (same as Fig. 2). Small circles, National Geophysical Data Center earthquake epicentres from 1963 to 1978; large circles, $M_b > 5.1$; stars, earthquakes whose mechanisms have been determined. Modified from ref. 8. M_b , earthquake magnitude.

developed in the middle of the 'spreading centre' when the spreading rate was very fast, suggesting that the Easter microplate is analogous³. This region of Pacific-Nazca opening may be just above such a speed limit, with dual active spreading centres bounding a growing microplate.

Although a microplate between dual spreading centres could originate in any of the several ways discussed above, its evolution depends on whether it is a transient or a stable phenomenon. One possibility is that two spreading centres are more effective than one in accommodating extremely fast plate separation and/or unusually intensive mantle convection and that this is a stable growing microplate with the potential to develop into a major oceanic plate. Arguments in favour of this hypothesis have focused on the possibility that less work might be required for dual spreading than for one superfast spreading centre³. However, faster spreading rates should lead to wider magma conduits and reduction in the viscous forces resisting spreading³⁹. Alternatively, the microplate could be a transient phenomenon. Perhaps it will eventually be welded to one of the major plates as one of the spreading centres fails, or perhaps its boundaries are more or less continuously rearranged so that there is usually a microplate of about this size in the area.

The propagating rift hypothesis provides the most straightforward explanation for why two spreading centres are currently active; thus, we interpret the microplate as a transient phenomenon between overlapping propagating and failing rifts on a grand scale, similar to Iceland (where there are dual rift zones and Surtsey appears to be at the tip of the southward-propagating south-east rift⁴⁰). Perhaps at this huge scale it takes several million years for the failing rift to cease spreading^{7,8,26,34,41} and during this transient microplate period, the failing rift curves strongly (perhaps adjusting azimuth by propagation) toward the propagator, as seen to a lesser extent in the Galapagos area²³. Thus, we concur with previous interpretations^{7,8} that the plate-boundary geometry is being rearranged by rift propagation and that the East rift will eventually pre-empt the West rift.

In our opinion, other very large (hundreds of kilometres) spreading centre jumps proposed previously⁴¹⁻⁴⁶ also resulted from large-scale rift propagation, perhaps initiated in this same area, which has been anomalously shallow for $> 30 \text{ Myr}$ ³⁴. Although mantle convection effects and/or superfast spreading

may be important for initiating such large-scale rift propagation, once initiated the propagation may continue away from this area (especially when plate motions are changing⁴⁷) and cause progressive large-scale spreading axis shifts. We interpret this microplate as the present-day analogue for the large-scale reorganization of the East Pacific⁴³ (and Indian Ocean⁴⁶) seafloor spreading system as the present EPR propagated north, gradually replacing the old Pacific-Farallon spreading system and reaching the North American continental margin at about the time and place that the continent began to break apart in the Gulf of California.

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Easter microplate evolution

J.-G. Schilling*, H. Sigurdsson*, A. N. Davis* & R. N. Hey†

* Graduate School of Oceanography, University of Rhode Island, Kingston, Rhode Island 02881, USA

† Scripps Institution of Oceanography, University of California at San Diego, La Jolla, California 92093, USA

Geochemical evidence confirms that there is current active spreading on both the East and West Rift zones of the Easter microplate, and northwards propagation of the East Rift with the active tip at 25°S. The East Rift is influenced by lateral flow of plume-derived material from a hotspot located beneath either Sala y Gomez or Easter Island. Spreading rate variation does not seem to be influential in controlling the composition of erupted basalts.

WE report on a rock-dredging cruise along the axis of the East Pacific Rise (EPR) between 22°S and 29°S along the boundaries of the Easter microplate (Fig. 1)^{1–4}. The region is of particular interest as the Pacific and Nazca Plates are diverging at a full-spreading rate of 180 km Myr⁻¹, the fastest currently active seafloor spreading rate on Earth⁵. The crest of the EPR is split into two branches which are spreading at very different rates and which form an intervening microplate^{1–4}. The elevation of the crest of the EPR shoals to a minimum of 2,100 m water depth near Easter Island^{6,7}, a proposed hotspot⁸ which may have influenced both the tectonics of the region by recurring rift jumps and the composition of volcanic products. The region is also extreme with respect to the recognized inverse correlation between spreading rate versus anomalous ridge crest elevation caused by the proximity of hotspots and associated mantle upwelling⁷: the slow-spreading ridge-centred Iceland hotspot is the other extreme in this relationship. The exact tectonic configuration and origin of the Easter microplate remains uncertain. Several models have been proposed to explain emerging data^{1–4,9–11}. Whichever model may prevail, the region provides a unique opportunity to study in a limited area the effect of spreading rates on melting and mixing conditions and homogenization of mantle heterogeneities possibly present

beneath mid-ocean ridges. So far, such studies have been limited to comparison of ridges from different oceans that may be underlain by mantle sources of possibly quite distinct histories. Our rock sampling was designed to study such effects by petrological and geochemical means as well as test proposed tectonic models. Here we present preliminary results obtained during a 1984 cruise aboard R/V *Endeavor* and a subsequent study of a first series of basaltic glasses, one per dredge haul, selected on the basis of freshness.

Exploration method

We used as a first guide the microplate boundaries proposed by Hey and co-workers^{3,4}, based on a recent SEABEAM and magnetic survey (Figs 1, 2). In contrast with previous interpretations, their model suggests that the East Rift is propagating northwards instead of north-north-east, and that the tip of the well-defined propagating rift is at ~25°S, 112°25'W instead of 23°20'S, 111°30'W, as proposed by Handschumacher and coworkers². The narrowing of the axial magnetic anomaly is explained by a young fast-propagating rift moving northwards into older crust of unknown age at a rate of ~150 km Myr⁻¹, with a constant total spreading rate of ~120 km Myr⁻¹. North of this propagator, we tentatively estimated the full rate of

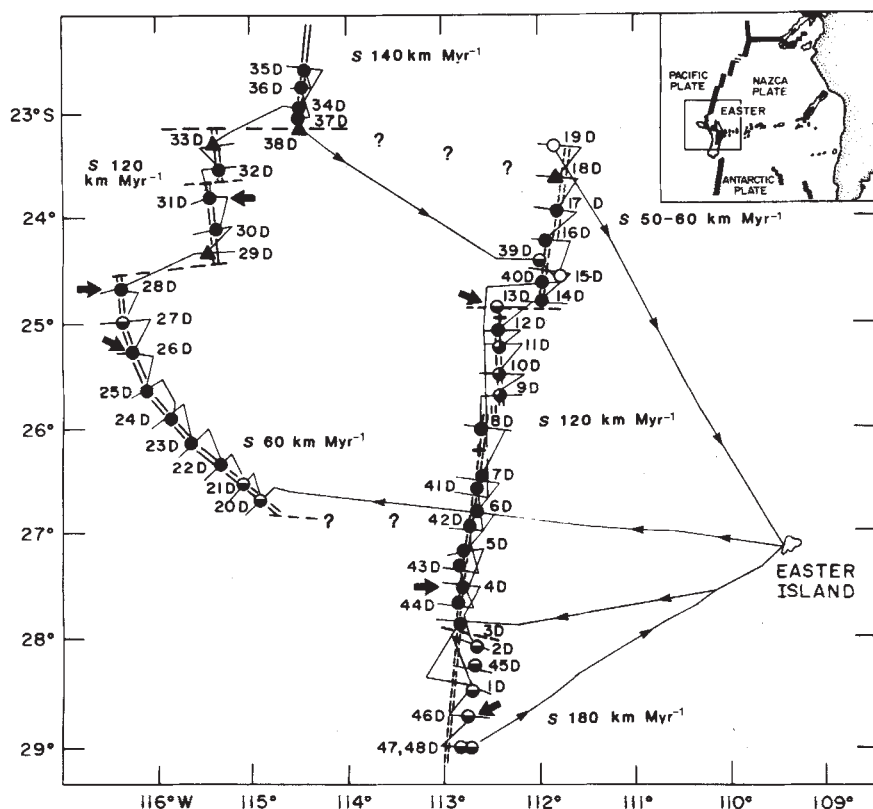


Fig. 1 Location of ship tracks and dredge hauls obtained during R/V *Endeavor* cruise EN-113. Full-spreading rates (s) of the various ridge segments proposed by Hey and co-workers⁴ are also indicated. Double lines show known location of rifts and double dashed lines inferred location. Question marks indicate uncertain location of fracture zones. See insert in Fig. 2 for locations of proposed propagating rift tips. Rock types collected indicated by: arrows, nepheline normative basalt; triangles, breccia and peridotite; circles, fresh glass; half filled circles, slightly altered glass; crosses, cruise Pascua 04 (ref. 4).

spreading to be 50–60 km Myr⁻¹, compared with 120–140 km Myr⁻¹ on the West Rift at the same latitude (23°S–24°30'S). South of the 24°30'S fracture zone, the West Rift curves north-west to south-east and the spreading rate may progressively decrease southwards, possibly as the result of the complex evolution of a leaky transform fault into a spreading centre which would involve the rotation of the microplate¹⁰ as well as rift propagation (Fig. 1). Simultaneous spreading of both the East and West Rifts is implicit in this model.

Before dredging, we ran 40–50-km long profiles across the plate boundaries, measuring bathymetry by seismic reflection (3.5 and 12 kHz) and total magnetic field intensity at 1-min intervals (Fig. 2). A portable X-ray fluorescence spectrometer (XRF) was used on board to analyse Fe, Cr, Mn and Ti in basalts immediately after dredge recovery, to explore the location of the tip of the proposed rift propagators in 'real time' and to study the possible effect of fracture zones on basalt composition. (It is now fairly well established that FeO* and FeO*/MgO content of basalts that erupted along mid-ocean ridges increase greatly near propagating rift tips^{12–16} as well as near some ridge-fracture intersections^{17–19}.) We first chose a relatively wide sampling interval to determine the broad first-order geographical trends in Fe, Cr, Mn and Ti. We then backtracked and dredged between the first series of stations to test and refine the first-order trend obtained on board. We carried out this second test only on the East Rift (see station number progression in Fig. 1; black dots and open circles in Fig. 3).

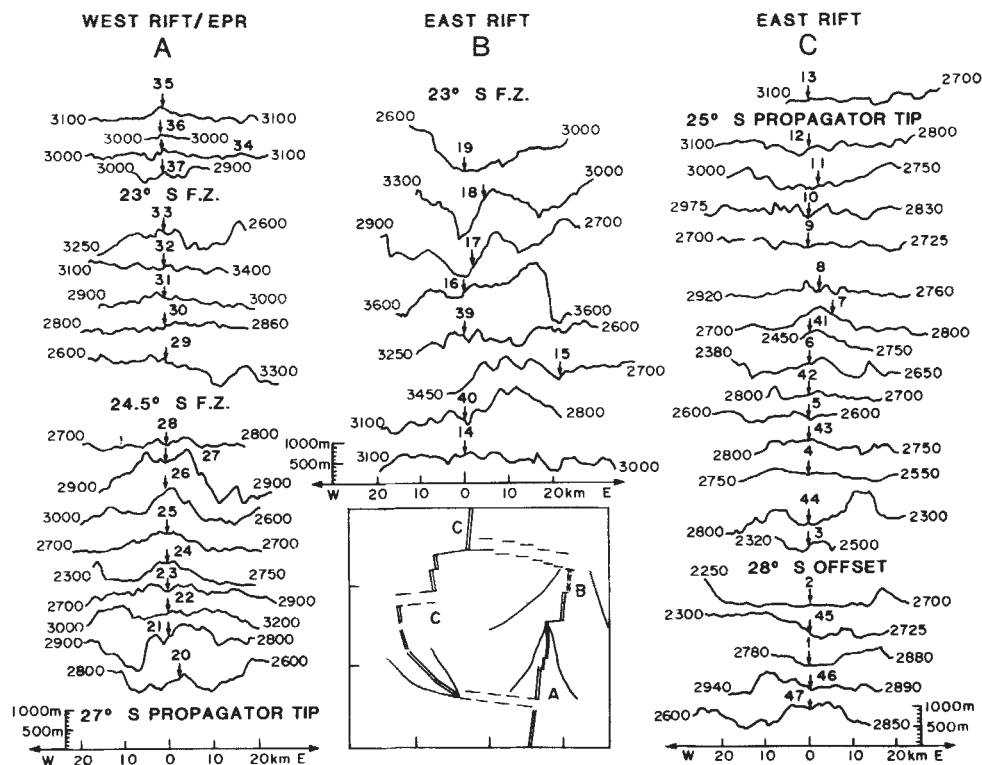
The nature of our rock recovery, including the distribution of fresh basaltic glasses (Fig. 1), confirms the gross features of Hey's preliminary tectonic model^{3,4,11}. Uncertainties in the position of the EPR axis remain, however, between 28°S and 29°S where the active rift might be 10–20 km west of our dredging, and on the northern end of the East Rift (north of station 17D) where a broad zone of deformation is suggested from the recovery of peridotites at station 18D and the abrupt discontinuity in the depth profile along the East Rift (Figs 2, 3). This evidence has been integrated with other geophysical evidence into a model which is discussed in detail elsewhere⁴ (see Fig. 2 insert).

East Rift

The first-order geographical trend in FeO*/MgO along the East Rift are shown in Fig. 3, which also illustrates the FeO* trend discovered using the XRF unit (black dots). There is a steady northwards increase in Fe content up to the propagating rift tip, accompanied by a deepening of the ridge crest and development of a rift valley (Fig. 2). This phenomenon was also observed on the 95.5°W rift propagator along the Galapagos Spreading Centre^{13,20}. North of the propagating rift tip, the FeO* content is significantly lower, and the elevation of the ridge crest is more typical of the EPR. In one dredge haul (13D) just north of the propagating rift tip, we recovered two types of basalts: an older type low in FeO*, comparable with basalts from the active ridge axis to the north east; and a fresh glassy type rich in FeO*. The older type is a quartz normative tholeiite, whereas the more recent basalt is nepheline normative (poorer in SiO₂, richer in Al₂O₃ and Na₂O) and may be the result of lower degrees of partial melting, as often found for ridge-flank magmas^{21–25}. This young basalt may represent the first melt associated with rift propagation.

Our preliminary profile also suggested a possible increase of FeO* south of 27°S, the nearest point to Easter Island, thus forming a V-shaped FeO* profile reminiscent of the one found on the Galapagos Spreading Centre^{12,13}, with a Fe minimum closest to the hotspot and Fe maxima near the propagating rift tips, one moving north, the other south. High-amplitude magnetic anomalies associated with the northern maximum are in agreement^{4,11}. Our subsequent test of this first-order trend confirmed the increase in FeO* northwards of 27°S, but also revealed an increased scatter in FeO* content about the preliminary trend south of 27°S (see open circles in XRF/FeO* trend in Fig. 3). FeO*/MgO variation, obtained by electron-probe analyses of basalt glasses after the cruise (Table 1), confirms the early XRF analyses on powdered basalt rocks made aboard the ship (Fig. 3), and supports the location of the tip of a rift at 25°S, but leaves open the possibility of a southwards propagating rift at 27°S. Evolved basalts with anomalously high FeO*/MgO ratio extend up to 100 km behind the 25°S propagat-

Fig. 2 Bathymetric profiles and locations of dredge hauls obtained during R/V *Endeavor* cruise EN-113. (See A, B, C here and Fig. 1 for location of the profiles across the spreading boundaries of the microplate.) The tectonic map (insert) shows the spreading boundaries of the Easter microplate recently proposed by Hey and co-workers⁴ which includes the recent geophysical and petrological evidence obtained during cruises Pascua 04 and EN-113. Double lines represent rifts; V-shaped lines represent the pseudo-faults with the proposed current propagating rift ribs at their apex; and double-dashed lines represent transform faults.



ing rift tip, reflecting the transient nature of magmatic processes associated with the propagation of this segment of the ridge. The width and height of this FeO^*/MgO anomaly is within the range observed along other propagating rift segments studied so far¹⁴, despite the fact that the rift propagating rate and spreading rate are in this case significantly higher (150 and 120 km Myr^{-1} , respectively). However, the ratios of propagation rate to spreading rate are similar and close to unity in all these cases.

As indicated above, the location of the axis of the EPR between 28° S and 30° S remains uncertain. The absence of fresh glass and the extent of palagonite and manganese oxide encrustation on pillow basalts recovered between 28° S and 29° S suggest that we were sampling a 1,000 to 10,000-yr-old sea floor, but not older than 100,000 yr. Topographical profiles (Fig. 2) suggest that the crest of the EPR is slightly west of our sampling, perhaps in direct continuation of the East Rift between 27° S and 28° S. This off-axis sampling may explain the scatter in FeO^* or FeO^*/MgO observed south of 28° S and does not exclude the possibility of southwards propagation of a rift as well. The crest of the EPR has been located at 30° S, just east of 112° W (H. Craig, personal communication). A major fracture zone offset must therefore be present between 29° S and 30° S. Thus, the tip of the inferred southward propagator may abut a major fracture zone, as is also the case for the 85° W Galapagos rift propagator^{12,13}.

West Rift

The western boundary of the Easter microplate was not sampled at the same density as the East Rift (Figs 1, 3). However, the overall distribution of fresh glasses along the West Rift (Fig. 1) and the apparent presence of two elongated, freshly frozen, lava lakes (24D and 25D) supports the hypothesis that active spreading is continuing. The lava lakes were evident from the flat nature of the axial valley (Fig. 2) and the recovery at these two stations of basalt sheet flows and fresh glass layers, sandwiched between flat basalt slabs. These features are similar to those observed²⁶ during submersible dives along elongated lava lakes on the axis of the EPR near 13° N. Simultaneous spreading on both the East and West Rifts is thus confirmed.

The FeO^* (XRF) and FeO^*/MgO variation on the West Rift and on the crest of the EPR north of the microplate is more

subdued and irregular (Fig. 3). However, there is a southwards increase in FeO^*/MgO along the south-east striking West Rift where rift propagating and decreasing spreading rate has been suggested^{3,4}. A reversal in the FeO^*/MgO trend occurs near the proposed tip at 26°45' S. This is also apparently the case on the 25° S propagator of the East Rift. Such maxima are also observed near the 95.5° W^{12,13} and Cobb^{14,15} propagators on the Galapagos and Juan de Fuca Ridge, respectively. It has been suggested that the distance of such FeO^*/MgO maxima to the actual tip of the rift propagator may be related to rift propagation rate and the length of associated transform fault zones¹⁴. A test of this idea will require additional data. However, we note that contrary to these other propagating rifts, the south-east rift propagator on the West Rift of the Easter microplate is converging toward the main EPR axis instead of diverging, and thus is penetrating a lithosphere that is progressively warmer instead of colder. This may perhaps account for the more subdued increase of FeO^* and FeO^*/MgO near the top of this propagator, relative to these other cases.

Basalt types and spreading rates

The basalts range mainly from quartz to olivine normative tholeiites on both the East and West Rifts of the microplate as well as on the EPR to the north and south. Nepheline normative basalts were found at six stations, three on the West Rift and three on the East (Fig. 1). These basalts are lower in SiO_2 and higher in Al_2O_3 and Na_2O content than the tholeiites and are all depleted in light rare-earth elements (REEs). They are also the least fractionated (Fig. 4) with Mg values ranging from 66 to 69.5, whereas most of the tholeiites have Mg values <66 (assuming an atomic ratio for $\text{Fe}^{3+}/\text{Fe}^{2+} + \text{Mg}^{2+} = 0.14$). In three of the six stations, the nepheline normative basalts coexist with quartz or olivine tholeiites.

The occurrence of nepheline normative glasses is not an unusual feature of the fast-spreading EPR south of the Equator. In a previous survey of the crest of the EPR between 5° S and 13° S²⁷, four stations out of ten were shown to contain nepheline normative basalts, and all the basalts were depleted in light REEs. In contrast, in our previous survey of the Mid-Atlantic Ridge axis from 79° N to 28° N²⁸ and 1° S to 47° S²⁹, with a full spreading rate ranging from <20 km Myr^{-1} on the Knipovich Ridge to 40 km Myr^{-1} in the South Atlantic, we encountered

Table 1 Major element concentrations and La/Sm ratios in basalts from the East Pacific Rise and East and West Rifts of the Easter microplate

Sample	Lat. °S	Long. °W	Depth (m)	Probe*										XRF‡				INAA§	
				SiO ₂	Al ₂ O ₃	FeO ^T	MgO	CaO	Na ₂ O	K ₂ O	TiO ₂	P ₂ O ₅	MnO	Mg ^{#†}	TiO ₂	Cr	FeO ^T	MnO	(La/Sm) _N
East Pacific Rise																			
EN113 35D-1	22.53	114.47	2912	50.13	15.69	10.53	8.19	11.48	2.54	.	1.55	0.07	0.18	61.7	1.58	215	10.82	0.19	0.51
EN113 36D-1	22.68	114.51	2950	50.55	14.72	10.31	7.45	11.83	2.84	.	1.59	0.11	0.16	60.0	1.65	228	10.71	0.20	0.57
EN113 34D-1	22.90	114.51	2975	51.17	15.15	9.21	8.38	12.42	2.40	.	1.21	0.04	0.16	65.3	1.11	256	9.59	0.16	0.44
EN113 37D-1	23.00	114.53	3035	50.68	14.11	11.81	6.80	11.27	2.85	.	1.96	0.10	0.20	54.4	1.95	147	11.46	0.20	0.51
EN113 38D-11	23.08	114.54	3125	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	0.35
East Rift Easter Microplate																			
EN113 18D-1	23.54	111.81	3532	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	0.60
EN113 17D-1	23.86	111.82	3905	50.38	14.73	10.64	6.89	12.11	3.01	0.05	1.97	0.22	0.17	57.3	1.71	178	10.85	0.18	0.62
EN113 16D-1	24.20	111.93	2950	50.55	15.68	8.61	8.30	12.16	3.24	0.10	1.49	0.24	0.18	66.6	1.37	206	9.67	0.15	1.02
EN113 39D-2	24.36	111.98	2898	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	0.54
EN113 15D-1	24.53	111.79	2975	50.78	12.69	14.10	6.00	10.53	2.89	0.05	2.93	0.36	0.36	46.9	2.64	158	13.24	0.21	0.64
EN113 40D-1	24.61	111.95	2825	50.23	15.33	9.31	8.43	13.10	2.54	.	1.11	0.10	0.16	65.2	0.89	276	9.11	0.15	0.44
EN113 14D-1	24.78	111.97	2630	51.41	14.93	9.57	7.72	11.87	2.80	0.02	1.45	0.21	0.09	62.6	1.42	158	10.36	0.18	0.59
EN113 13D-1	24.86	112.45	2948	48.91	17.11	8.70	8.15	11.75	3.54	.	1.50	0.17	0.04	66.0	1.27	505	10.16	0.18	0.39
PA04-12-A	24.98	112.42	3264	50.25	13.41	13.39	5.95	10.07	3.08	0.15	2.57	0.32	0.30	47.9	.	.	.	.	0.84
EN113 12D-1	25.03	112.41	3255	50.57	13.21	13.30	5.68	10.20	3.01	0.12	2.66	0.36	0.17	47.0	2.23	112	12.11	0.22	0.94
EN113 11D-1	25.24	112.38	3158	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	1.15
EN113 10D-2	25.47	112.39	2970	50.83	13.16	13.66	5.54	10.16	2.97	0.10	2.74	0.33	0.27	45.7	2.38	55	12.10	0.20	0.93
EN113 9D-1	25.66	112.38	2865	50.62	13.56	12.62	6.04	10.66	2.93	0.11	2.72	0.35	0.18	49.8	2.55	92	12.67	0.19	0.93
EN113 8D-1	25.98	112.55	2668	51.04	14.36	11.50	6.97	10.39	2.85	0.10	2.16	0.22	0.18	55.7	1.99	176	11.42	0.19	0.96
PA04-11-A	26.27	112.62	2425	50.11	14.60	10.84	6.82	11.48	2.96	0.23	2.09	0.29	0.23	56.6	.	.	.	.	1.10
EN113 7D-1	26.46	112.57	2272	49.75	15.65	10.30	6.93	10.37	3.03	0.37	2.57	0.30	0.17	58.2	2.13	195	10.42	0.16	1.71
EN113 41D-1	26.58	112.65	2282	50.42	15.40	10.12	7.02	11.41	3.06	0.20	2.20	0.28	0.19	59.0	2.08	195	10.87	0.18	1.39
EN113 6D-1	26.81	112.64	2362	49.81	16.27	10.09	7.14	10.18	3.02	0.45	2.54	0.30	0.15	59.5	2.23	153	10.37	0.16	1.94
EN113 42D-1	26.92	112.70	2590	50.24	15.37	9.66	7.50	11.35	2.92	0.19	2.04	0.31	0.21	61.7	1.84	239	10.52	0.18	1.26
West Rift Easter Microplate																			
EN113 33D-1	23.25	115.43	2815	.	.	.	.	.	.	.	.	.	.	.	1.35	165	10.33	0.18	0.62
EN113 32D-1	23.48	115.38	3270	50.56	14.24	11.22	7.36	11.62	2.64	0.02	1.95	0.16	0.19	57.6	1.79	220	11.44	0.20	0.69
EN113 31D-1	23.77	115.47	2660	50.51	14.70	10.75	7.78	11.77	2.67	.	1.45	0.08	0.19	60.0	1.51	217	11.16	0.21	0.65
EN113 30D-1	24.11	115.41	2800	50.34	15.11	10.34	7.25	11.28	3.09	0.01	1.93	0.28	0.20	59.2	0.90	293	9.27	0.15	0.35
EN113 29D-1	24.31	115.47	2692	49.79	15.01	10.42	7.70	11.71	2.98	0.04	1.60	0.30	0.19	60.5	.	.	.	.	0.71
EN113 28D-1	24.64	116.42	2740	49.31	16.43	9.01	8.55	12.31	3.02	.	1.32	0.02	0.16	66.3	1.15	236	9.61	0.16	0.40
EN113 27D-1	24.99	116.36	2060	50.63	14.78	9.84	7.76	12.44	2.64	0.07	1.54	0.09	0.17	62.0	1.33	267	9.01	0.16	1.10
EN113 26D-1	25.28	116.27	2052	47.90	17.96	9.51	9.92	11.36	2.79	.	0.82	0.01	0.15	68.4	0.78	317	10.85	0.18	0.43
EN113 25D-1	25.66	116.13	2240	50.60	14.57	10.69	7.43	11.72	2.99	0.04	1.65	0.17	0.24	59.0	1.66	158	11.15	0.19	0.83
EN113 24D-1	25.90	115.86	2212	50.36	14.50	10.90	7.28	11.67	2.96	0.07	1.73	0.17	0.24	58.1	1.75	126	11.43	0.19	0.96
EN113 23D-1	26.13	115.64	2608	50.42	14.60	10.94	7.28	11.90	2.92	0.05	1.77	0.15	0.26	58.0	1.65	168	11.20	0.19	0.88
EN113 22D-1	26.35	115.32	2788	50.60	13.75	12.49	6.56	10.83	2.91	0.08	2.21	0.19	0.30	52.1	1.96	106	11.24	0.19	0.95
EN113 21D-1	26.52	115.09	2705	50.93	13.94	11.52	6.88	11.44	2.84	0.06	1.73	0.18	0.22	55.3	1.48	131	10.82	0.18	0.86
EN113 20D-1	26.70	114.92	2918	49.88	14.71	10.47	7.46	12.35	3.04	0.08	1.76	0.19	0.18	59.6	1.60	226	9.11	0.16	1.09
East Pacific Rise																			
EN113 5D-1	27.21	112.77	2632	50.08	15.72	9.21	9.21	12.01	2.41	.	1.07	0.12	0.18	67.5	0.99	261	9.82	0.16	0.54
EN113 43D-1	27.30	112.81	2438	50.48	14.80	9.96	7.46	11.96	2.77	0.09	1.69	0.27	0.18	60.8	.	.	.	.	1.03
EN113 4D-1	27.53	112.76	2520	47.29	16.59	11.23	10.59	10.24	2.83	.	1.39	0.12	0.18	66.2	1.26	285	11.91	0.19	0.59
EN113 44D-1	27.64	112.84	2522	50.19	15.70	8.73	8.21	12.55	2.75	0.06	1.44	0.26	0.23	66.1	1.30	250	9.16	0.15	1.03
EN113 3D-1	27.88	112.81	2300	49.64	16.34	9.43	8.23	10.99	2.93	0.19	1.87	0.20	0.14	64.4	1.68	187	9.62	0.15	1.44
EN113 2D-1	28.08	112.66	2784	50.39	14.43	11.13	6.43	11.15	3.15	0.19	2.24	0.35	0.25	54.5	1.95	134	10.89	0.18	1.35
EN113 45D-1	28.29	112.66	2758	52.23	13.55	12.57	5.50	9.82	2.92	0.16	2.09	0.43	0.32	47.6	2.09	101	12.55	0.22	0.87
EN113 1D-1	28.48	112.65	2950	.	.	.	.	.	.	.	.	.	.	.	1.57	153	11.12	0.19	0.71
EN113 46D-1	28.72	112.73	2750	49.25	17.34	7.93	8.71	12.02	3.25	0.05	1.22	0.24	0.14	69.5	1.30	282	8.60	0.15	0.68
EN113 47D-2	29.01	112.79	2488	50.62	14.68	10.49	7.45	11.55	3.13	0.02	1.83	0.30	0.25	59.5	.	.	.	.	0.64
EN113 48D-1	29.02	112.70	2448	50.75	14.57	10.61	7.14	10.99	3.09	0.05	2.26	0.32	0.23	58.2	2.04	165	11.80	0.20	0.62
Probe Standards																			
VG-A99 Reference standard				51.31	12.70	13.32	5.13	9.35	2.65	0.76	3.97	0.46	0.21						
standard deviation				0.50	0.25	0.34	0.15	0.20	0.14	0.10	0.22	0.07	0.05						
VG-A99 Accepted value				50.90	12.97	13.18	5.18	9.38	2.73	0.80	3.89	0.41	0.19						
VG-2 Reference standard				50.91	14.09	11.66	6.98	11.15	2.68	0.16	1.77	0.28	0.21						
standard deviation				0.45	0.19	0.25	0.17	0.23	0.16	0.05	0.12	0.03	0.05						
VG-2 Accepted value				50.81	14.06	11.84	6.71	11.12	2.62	0.19	1.85	0.20	0.22						

All concentrations in weight % except Cr in p.p.m.; FeO^T is total iron as FeO.

* Averages of 9–12 spot electron microprobe analyses on at least three glass chips per sample. Microprobe operating conditions and methods for basalt glass analysis are the same as Sigurdsson⁴⁹ except counting times were 20 s and Corning synthetic glass 'W', USGS fused basalts BCR-1 and AGV-1 were used as primary standards for Mn, Ca and Al, respectively.

† Mg[#] = Mg²⁺/Mg²⁺ + Fe²⁺ atomic ratio assuming an atomic ratio of Fe²⁺/Fe²⁺ + Fe³⁺ = 0.14.

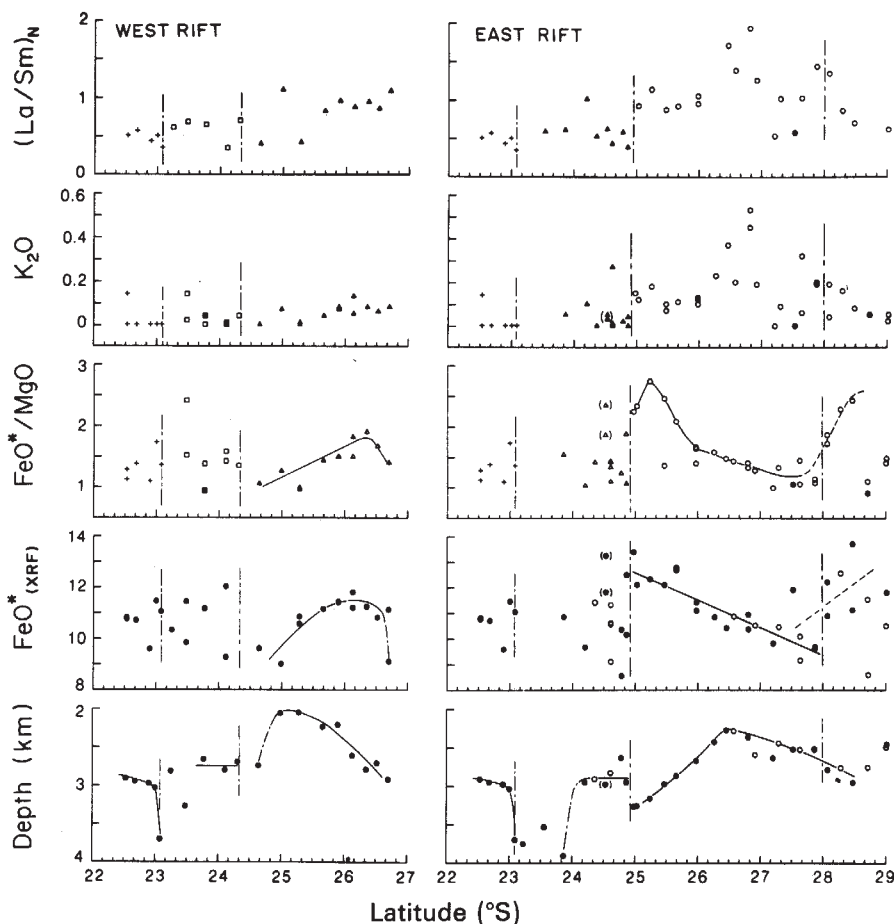
‡ Averages of 3 XRF analyses of the basalt interior powders. A portable X-ray fluorescence spectrometer (Hankison Model 2501 Portaspec) was used for shipboard analysis of Fe, Ti, Mn and Cr. Method will be reported by Davis *et al.* (in preparation). Estimated precision and accuracy are (in %) ±4.0 and 5.2, ±2.7 and 9.4, ±9.2 and 11.9 and ±18.6 and 37.1 for FeO^T, TiO₂, MnO and Cr respectively.

§ La/Sm ratios in basaltic glasses were obtained by the same routine INAA method as reported by Schilling *et al.*²⁸.

|| Average and one standard deviation for 46 and 14 microprobe analyses of test standards VG-99 and VG-2 respectively. Accepted compositions of the standards were determined by wet chemical analyses from Jarosewich *et al.*⁵⁰.

nepheline normative basalts in only 3 of >200 stations. Two were strongly enriched in light REEs and associated with off-ridge hotspots (35° N, Great Meteor and 16° S, St Helena) and one was picritic and unusually strongly depleted in light REEs (just south of the Hayes Fracture Zone). Out of 28 stations on the Galapagos Spreading Centre (60 km Myr⁻¹ spreading rate),

Fig. 3 Latitudinal variation of depth and composition of basalt glasses dredged along the East Rift (right) and West Rift (left) bounding the Easter microplate. Black dots and open circles in the depth and FeO* (XRF) profiles represent first and second dredge sampling sequence (see text). For other profiles, ridge segments spreading at different rates (see Fig. 1) are shown by different symbols: Left (West Rift)—cross, 140 km Myr⁻¹; open square, 120 km Myr⁻¹; open triangle ~0–60 km Myr⁻¹. Right (East Rift)—cross, 140 km Myr⁻¹; open triangle, 50–60 km Myr⁻¹; open circle, 120 km Myr⁻¹, including segment south of the microplate (28° S–29° S) where our sampling is off the ridge axis and spreading rate at this time is uncertain. The FeO* (XRF) trend is from whole-rock powders. Other trends are from a first series of basalt glasses selected from each dredge haul on the basis of freshness. A study of variability within each dredge haul is now in progress.



Myr⁻¹ (26D, 28D and 31D), two at 180 km Myr⁻¹ (46D and 4D), and we have already commented on station 13D beyond the 25° S propagating rift tip where the spreading rate is probably very slow. The low SiO₂ nepheline normative basalts may represent rapid segregation of melts from greater depths without significant mixing or residence time in shallow magma chambers possibly underlying these EPR ridge segments. It also suggests that if well mixed, steady-state-like magma chambers are present beneath the fast-spreading EPR as commonly assumed, they are not continuous. Finally, the commonly held notion of increasing basalt alkalinity with decreasing spreading rate^{30,31} does not seem to be justified.

Our preliminary petrological study indicates little difference in the range of petrological type between the East and the West Rifts, or the EPR segments north or south of the microplate, or with proposed spreading rates (Fig. 1). They all overlap and follow the same general fractionation trend, which is not particularly different from slower spreading ridges (Fig. 4).

Finally, we note that basalts on the East Rift from the two stations (6D and 7D) that are closest to Easter Island and most enriched in K₂O and light REEs, are also distinctly lower in CaO/Al₂O₃ for their intermediate Mg values (58–61). These features suggest early saturation and removal of clinopyroxene. Basalts from these two stations are also displaced toward the plagioclase apex in Fig. 4, and are off the general fractionation trend for the Easter microplate, suggesting that a wider pyroxene stability field also exists. The same situation was observed on the Galapagos Spreading Centre on the segment closest to the Galapagos hotspot^{13,32}.

Hotspot influence

Preliminary data on K₂O and La/Sm variations along the East Rift of the microplate culminate around 27° S, where the elevation of the axis reaches a maximum. This segment of the East Rift is also closest to Easter Island (Fig. 3) and the morphology of the ridge axis is domed and highly constructional (Fig. 2).

On the other hand, on the West Rift and on the EPR north of the microplate, both the K₂O content and the La/Sm are more typical of normal mid-ocean ridge basalts (MORBs) ((La/Sm)_N < 1, K₂O < 0.1 wt%) (Figs 3 and 5).

The La/Sm profile on the East Rift is clearly decoupled from that of FeO/MgO* and its gross feature is likely neither to be the result of shallow depth fractional crystallization, nor the result of smaller degrees of melting (Fig. 3). The locations of the few nepheline normative basalts encountered with low SiO₂ and high Al₂O₃ and Na₂O, which could reflect smaller degrees of melting and derivation from greater depth, show no relation with that of La/Sm (Fig. 1). Furthermore, a plot of TiO₂ and P₂O₅ with latitude using data from Table 1 would reveal a complex pattern intermediate between that of FeO*/MgO and (La/Sm)_N. This is to be expected because these two incompatible elements are normally affected by both magmatic processes (extent of partial melting and fractional crystallization, as reflected by the FeO*/MgO variation) and mantle heterogeneities (as reflected by the (La/Sm)_N variation). These incompatible element variations strongly suggest that the anomaly in La/Sm on the East Rift is mantle-derived and related to the influence of a hotspot located east of the microplate, either the Easter hotspot⁸ or the Easter hotline³³. This is supported by high ⁸⁷Sr/⁸⁶Sr and ³He/⁴He and low ¹⁴³Nd/¹⁴⁴Nd isotope analyses of two glasses collected during the Pascua expedition^{34,35} (see the two crosses in Fig. 1).

The slight increase of K₂O and La/Sm south-east on the West Rift (Fig. 3), which is accompanied by a slight increase in FeO*/MgO, could in part be accounted for by either shallow depth fractional crystallization, slightly smaller degrees of melting, or by the fact that the ridge is striking south-east and is moving closer to the East Rift and the alleged hotspot.

The combined La/Sm profile for the EPR between 18° S and 34° S, including the microplate (Fig. 5), shows that the width of the La/Sm anomaly is of the order of 350 km. The anomaly is spike-like and irregular and characterized by large local disper-

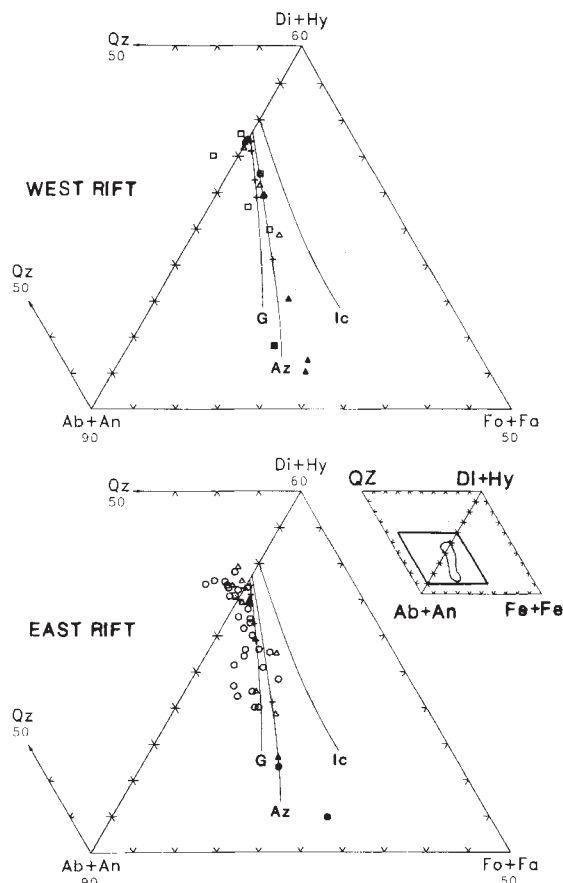


Fig. 4 CIFW normative ternary plots (wt %) for basalt glasses dredged during cruise EN-113. *a*, East; *b*, West. Symbols define ridge segments spreading at different rates as indicated in Fig. 3 (see also Fig. 1). *Ic*, *Az* and *G* are best-fit liquid lines of descent for other MORBs from segments spreading at full rate of: 20 km Myr⁻¹ (MAR 53° N–69° N, ref. 28); 40 km Myr⁻¹ (MAR, 28° N–52° N, ref. 28); and 60 km Myr⁻¹ (Galapagos Spreading Centre, 83° W–102° W, ref. 13), respectively. The best-fit lines were obtained by a method described by Bryan and Dick⁴⁶.

sion, which we have shown is characteristic of the influence of off-ridge hotspots on the geochemistry of adjacent ridge axes²⁹. We have shown that for ridges with a full-spreading rate of 20–60 km Myr⁻¹, there is an inverse relationship between either the width of geochemical anomalies on migrating ridge segments (W), or associated anomalous elevation (ΔE), and distance (y) to nearby hotspot influencing these ridge segments; namely $W = 1,010 - 24.5 y^{1/2}$ and $\Delta E = 2.42 \times 10^{-3} W$, with W , y and ΔE in km³⁶. Taking these two empirical relationships at face value and using $W = 350$ km, we calculate that the hotspot should be located 725 km east of the East Rift (as this rift is geochemically the most affected of the two). The predicted topographical anomaly around 27° S should be 0.85 km above the normal mid-ocean ridge depth (2,900 m), or 2,050 m; this is in good agreement with the observed depth of 2,100 m (Figs 2, 3).

This model places the hotspot beneath Sala y Gomez, as also recently proposed by Duncan and Hargraves³⁷ and Okal and Cazenave³⁸ on the basis of hotspot tracks and plate reconstructions, and not beneath Easter Island⁸. The only rare-earth abundance pattern available in basalts from Sala y Gomez is the most enriched in light REEs among basalts of similar bulk composition observed along the so-called Easter hotline, including Easter Island and the seamounts located east of Sala y Gomez³⁵. There is also a suggestion that the ¹⁴³Nd/¹⁴⁴Nd ratio increases from Sala y Gomez, Easter Island and the East Rift of the microplate, and that the ⁸⁷Sr/⁸⁶Sr ratio tends to decrease^{35,39}. These observations support the hypothesis of a subcrustal lateral flow between

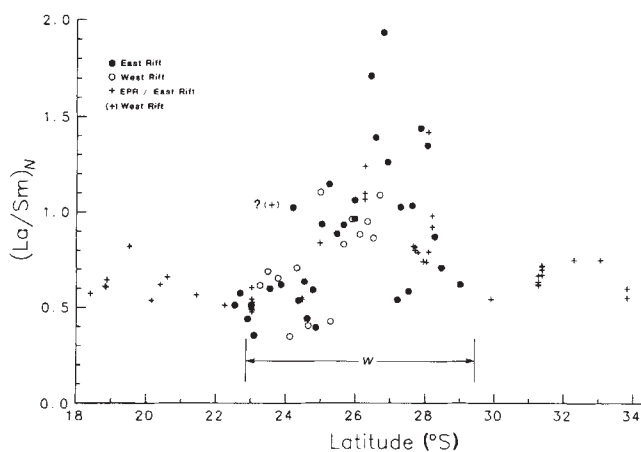


Fig. 5 Latitudinal variations of La/Sm ratio (normalized to chondrites) along the axis of the EPR from 18° S to 34° S, including the East and West Rifts of the Easter microplate. Data sources from: filled and open circles, this work; crosses, refs 27, 47, 48 and unpublished analyses from this lab including samples from SIO Pascua 03 and 04 expeditions (samples provided by J. D. Macdougall and H. Craig) and University of Miami cruise G27202 (samples provided by E. Bonatti). Width of geochemical anomaly (W) is discussed in text.

the proposed Sala y Gomez hotspot and the westwards-migrating EPR, and accompanied binary mixing with the large-ion lithophile element-depleted asthenosphere, as is also apparent for other off-ridge hotspots^{13,29,40}. This lateral flow would also roughly coincide with the so-called Easter Fracture Zone. Any segment of the Easter Fracture Zone subject to a small component of extension could conceivably leak and generate volcanism along the flow line, producing the recent seamounts, Easter Island and the so-called Sala y Gomez Ridge⁴¹ (a broad shallow zone punctuated with many seamounts east of the microplate; see Fig. 1 insert).

In addition to the empirical width (W) versus distance (y) relationship discussed above, we have also shown that the width of a hotspot-related geochemical anomaly along ridges may also be inversely related to spreading rate (S) ($W \propto 1/S$)³⁶. The distance of the hotspot could easily be reduced by a factor of 2–3, as the East Rift is spreading at 120 km Myr⁻¹ where the La/Sm anomaly peaks, or 50–60 km Myr⁻¹ north of the propagator, whereas the empirical relationship between W and y was obtained for ridge segments with full-spreading rates of 20–60 km Myr⁻¹. Thus, the hotspot could be located closer to or beneath Easter Island. In this case, as within the reference frame of a fixed hotspot, the Pacific–Nazca plate boundary is moving from the Easter Island hotspot in a 280° direction⁴², and the geochemical anomaly maximum on the East Rift falls on the same vector, it suggests that the lateral flow toward the EPR would also strike 280° (see, for example, ref. 40). Furthermore, since the Nazca Plate is moving essentially eastward with respect to the fixed hotspot, the track left on the Nazca Plate by constructional volcanism associated with the discharge of this lateral flow at the migrating EPR axis, should strike between 270°–280°, and thus could correspond with the so-called Sala y Gomez Ridge. Thus, it is conceivable that the Sala y Gomez Ridge could reflect such track of constructional volcanism instead of having been formed along a leaky fracture zone as suggested by Clark and Dymond⁴¹. Resolution of the topography in the area and uncertainties in the absolute plate motions do not yet permit us to choose among these various alternatives.

Whether the hotspot is beneath Sala y Gomez or Easter Island, it is conceivable that the plume flow, although directed predominantly westwards toward the migrating EPR, could also more recently have been partly channelled eastwards along a zone of slight plate divergence as the hotspot is becoming increasingly intraplate. This is supported by the observation that

the influence of the EPR sink is likely to decrease as it migrates westwards³⁶, and by much evidence that plate movements in the region have been repeatedly reorganized during the past 25 Myr⁴³. These movements could have led to a slight divergence of the plates north and south of the Easter Fracture Zone. Thus, we believe that this channel flow model is a viable alternative to the previous model which calls for a hotline along the Easter Fracture Zone, consisting of two narrow convective rolls lines up parallel to the return spreading flow lines³³. The two models need not be mutually exclusive.

Thus, the exact location of the hotspot which influences the geochemistry of the East Rift of the microplate remains an open question. Additional evidence, including isotope data and a better definition of spreading rates and topography around the Easter microplate are needed to resolve the question.

In conclusion, our preliminary petrological-geochemical results and the morpho-tectonic configuration of the Easter microplate are reminiscent in many ways of that of the Galapagos region in its early stage of development, perhaps at the time of the proposed southwards rift jump^{44,45}. However, the Easter hotspot is now even more remote from the westwards-migrating EPR than the Galapagos hotspot is with respect to the Galapagos Spreading Centre. The analogy is evident from the nearly symmetrical shoaling of ridge elevation, the La/Sm increase, the possible decrease in FeO*/MgO at ~27° S on the

East Rift and the position of the 25° S rift propagator relative to the probable hotspot position. If the analogy is essentially correct, another rift propagator may have extended southwards along the EPR south of the Easter microplate, with the tip abutting against a major 29° S–30° S fracture zone offset. This remains to be tested by additional geophysical surveys to locate accurately the rift south of 28° S, and additional sampling of the zero-age axis.

The speculation^{2,4,10,11} that spreading of the West Rift axis of the Easter microplate might cease in the future and leave active only the East Rift closest to the Easter hotspot appears justified from the fact that basalts from the West Rift are comparatively less evolved than on the East Rift.

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Single-channel currents of an intercellular junction

Jacques Neyton and Alain Trautmann

Laboratoire de Neurobiologie, Ecole Normale Supérieure, 46 rue d'Ulm, 75005 Paris, France

We have used a double whole-cell patch-clamp system to make the first quantitative recordings of the single-channel current from an intercellular junction, presumably a gap junction. The junctional channel has various conductance states and discriminates poorly between cations and anions. It seems to change slowly from one conductance state to another.

IN many tissues there is a system of direct cell-to-cell communication that does not proceed through the extracellular space. In all the preparations studied so far, this intercellular communication has been shown to be ensured by specialized structures, the gap junctions, where the apposed membranes of two cells, separated by a 3.5-nm space (the gap), are linked by a lattice of channels (see refs 1, 2 for review). The junctional channels provide a direct pathway for both electrical and metabolic

communications between coupled cells. They are large enough to allow the flux of molecules up to 2 nm in diameter^{3,4}. Their conductance has not yet been measured, although quantum jumps of conductance have been observed under conditions that gave only qualitative information⁵.

Here, we report the use of a double patch-clamp system to study the electrical coupling in pairs of cells isolated from rat lacrimal glands. The voltage and current were controlled in both

cells. The signal-to-noise ratio was such that we could observe quantal junctional conductance changes which were probably caused by the opening and closing of single junctional channels. With this technique, the ionic composition of the intracellular contents of both cells could be effectively controlled and the ionic selectivity of the junctional channels could thus be determined.

Experimental approach

The enzymatic dissociation of rat lacrimal glands⁶ produces single cells as well as pairs or small clusters of still-interconnected cells⁷. Our experiments were performed on freshly isolated pairs of cells. Two patch-clamp systems were used to obtain simultaneous whole-cell, tight-seal recordings⁸ from the two paired cells. The background noise of the system was minimized by using small cells (15–20 μm in diameter) with capacitances of ~ 10 pF and nonjunctional membrane resistances of several gigaohms. Figure 1a shows the equivalent circuit for a pair of cells, C_1 and C_2 . In principle, if the holding potential of C_2 is maintained perfectly constant while that of C_1 is stepped by V mV, the current change ΔI_2 in C_2 will be precisely the current I_j flowing through the intercellular junction and the conductance of the junction would be $G_j = I_j/V$. Therefore, in theory the presence of nonjunctional channels in C_1 and C_2 can be ignored as the transjunctional current is measured in C_2 , that is, a cell where the membrane potential is kept constant. In practice, because the access resistances r_1 and r_2 to the cells were not negligible, the transjunctional current and voltage differed from ΔI_2 and V , respectively. The following estimates of G_j take into account the corrections (see Fig. 1 legend) imposed by the series resistance of the electrodes, and by the nonjunctional membrane resistance of C_2 .

A depolarizing pulse V applied in C_1 evokes a noisy outward current ΔI_1 (Fig. 1b). This current is the sum of the current passing through the junction and that flowing through channels of the nonjunctional membrane of C_1 . The latter channels have previously been shown to be voltage- and Ca-dependent⁷. Although the holding potential of C_2 (V_2) is maintained constant, an inward current (ΔI_2) is induced in this cell by the imposition of a transjunctional potential difference.

The state of the electrical coupling between lacrimal cells at the beginning of experiments and its stability throughout the experiments were examined using the different solutions A–E of Table 1, that is, solutions containing a high K and a low Ca concentration at pH 7.2. The initial value of the conductance of the junction G_j was measured 1–2 min after the second whole-cell recording was obtained. This delay was necessary to measure accurately the two series resistances. Initial values of G_j fall in three groups. In most of the cell pairs (63%) the initial G_j value was >30 nS and the average conductance was 58 ± 25 nS (mean $\pm$ s.d., $n = 16$). A second group of cell pairs (25%) showed a low initial G_j value (range 1–15 nS). In the remaining 12% of the pairs, the cells were completely uncoupled from the beginning, probably as a result of the dissociation procedure. The stability of the coupling was followed in 15 pairs of cells that were initially strongly coupled (first group). Six of these pairs became rapidly uncoupled in less than 5 min. The cause of this spontaneous fall in the junctional conductance is as yet unknown. It has been shown previously that a rise in the intracellular concentrations of Ca^{2+} ions^{9,10} or of protons^{10–14} could cause the closure of junctional channels. However, the fall in G_j that we observed was probably not caused by a decrease in either pCa or pH because it also occurred in pairs of cells in which the Ca or proton concentrations were tightly controlled (solutions C and D). The other nine cell pairs remained strongly coupled for more than 10 min; their coupling conductance decreased by a factor of <2 during this time, two of them even displaying a temporary increase in coupling conductance.

Voltage dependence

In contrast with some other preparations (refs 15, 16; see ref. 17 for review), the open junction between two strongly coupled

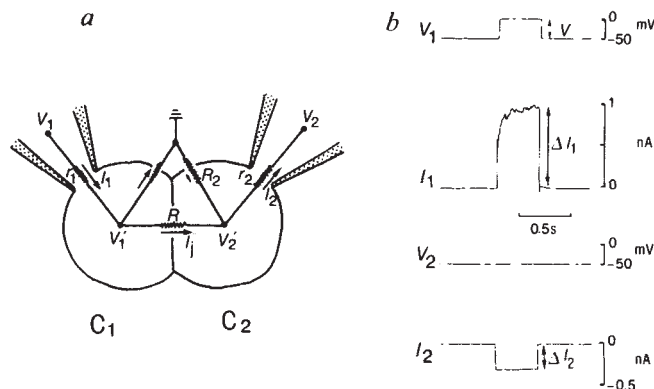


Fig. 1 a, Equivalent circuit of a coupled cell pair, C_1 and C_2 ; b, simultaneous recording of the command voltages (V_1 and V_2) and the recorded currents (I_1 and I_2) in a pair of cells during a voltage jump in C_1 . a, I_1 , current flowing through electrode 1, whose access (or series) resistance is r_1 . The difference between the command voltage V_1 and the effective holding potential V_1' is equal to $r_1 I_1$. V_2 , V_2' , I_2 and r_2 are defined similarly for the second cell. To estimate the conductance of the junction G_j , V_1 and V_2 are initially fixed at the same holding value. In most of the experiments, the common holding potential was in the range of -40 to -70 mV, the holding currents were negligible at these potentials so that V_1' and V_2' were equal to their command value. A command voltage jump V applied to C_1 induces current changes ΔI_1 and ΔI_2 in the two electrodes. Therefore, the voltage jump really applied to the junction has the amplitude $V_j = V_1' - V_2' = V - (r_1 \Delta I_1 - r_2 \Delta I_2)$ where, as seen in b, ΔI_1 and ΔI_2 have opposite signs; therefore the errors are additive. As V_2 changes by $r_2 \Delta I_2$, during the voltage jump in C_1 , a fraction of the transjunctional current I_j passes through the membrane of C_2 (small arrow). If R_2 is the nonjunctional membrane resistance of C_2 , and if the voltage change in C_2 is small enough not to activate voltage-dependent channels, $I_j = \Delta I_2(1 + r_2/R_2)$. The above values of V_j and I_j allow one to calculate $G_j = I_j/V_j$. b, In this example, $r_1 = 5$ M Ω , $r_2 = 12$ M Ω . The magnitude of the voltage drop in the series resistance r_1 changes with time as ΔI_1 is time-dependent, caused by the activation kinetics of the voltage- and Ca-dependent channels⁷. However, the time-dependent variation in the transjunctional voltage that is created by the voltage drop in the series resistance r_1 is $<10\%$. This conclusion can be drawn from either a simple calculation (based on the principles outlined for a), or from the examination of the time course ΔI_2 . The current flowing through the junction is equal to ΔI_2 , as $r_2/R_2 < 10^{-2}$. In this experiment, the pipettes were filled with solution A.

Methods. Rat lacrimal glands were dissociated as described previously⁶. Briefly, the exorbital lacrimal glands were incubated successively in trypsin, EGTA and collagenase, submitted to a mild pipetting and kept at 37°C in culture medium until the experiment, which was performed at room temperature in mammalian saline (see ionic composition in Table 1). Cells obtained by this procedure have input resistances of several gigaohms, that is, values 20–100 times larger than the resistance of the junction. The micropipettes were filled with the solutions given in Table 1 and had resistances of 2–4 M Ω when measured in the bath. The series resistances r_1 and r_2 were estimated in each cell from the parameters used to cancel the capacitive surge of current at the beginning of a voltage jump⁸ simultaneously applied to both cells, so that no current flowed through the junction. The values of r_1 and r_2 (range 5–20 M Ω) were repeatedly checked during the experiment, and suction was occasionally reapplied if an electrode started to clog.

Table 1 Ionic composition (mM) of the extracellular bath solution and of the solutions used to fill the micropipettes

Solution	KCl	NaCl	EGTA	CaCl ₂	pCa	MgCl ₂	HEPES	pH
Bath	5	140	0	1	3	1	5	7.2
A	140	0	5.5	0.5	8	2	5	7.2
B	140	0	0.5	0	?	2	5	7.2
C	84	0	20	2	8	2	30	7.2
D	130	0	5.5	0.5	8	2	30	7.2
E	130	0	0.5	0	?	2	30	7.2
H	0	140	5.5	0.5	8	2	5	7.2
I*	35	0	1.4	0.13	8	0.5	5	7.2

* Also containing 158 mM mannitol.

lacrimal cells shows no voltage dependence (Fig. 2a, circles). In this experiment, the transjunctional current was initially linearly related to the transjunctional voltage (circles). When a spontaneous uncoupling develops slowly and irreversibly, however, a voltage sensitivity of the junctional conductance often appears (Fig. 2a, triangles). In some cases, this voltage sensitivity gives rise to current relaxations during transjunctional voltage jumps (Fig. 2b). In contrast to the slow irreversible uncoupling mentioned above, these current relaxations are reversible, shown by the similarity between the initial current changes produced by two successive voltage jumps (Fig. 2b). Relaxations of the transjunctional current in both directions, corresponding to a current increase or decrease, can be observed, depending on the polarity of the transjunctional potential (Fig. 2c).

In summary, as judged from the voltage dependence of the junctional conductance, the two faces of the junction are symmetrical at the beginning of a recording. This is not surprising in view of the identical role played by the different cells in an acinus. However, an asymmetry often develops with time as the cells uncouple. It may be that the same factors are responsible for the voltage dependence and for the closure of the junction, and that in most cases these factors do not appear symmetrically in both cells.

Current through one channel

Before the irreversible closure of the junction takes place, it is possible to observe the current flowing through the remaining open channels of the junction provided that the background noise of the double whole-cell recording is low enough (Fig. 3). Current measured in cell 2 in response to voltage jumps in cell 1 sometimes shows no variation at all (Fig. 3a, b). As expected from the experimental diagram given in Fig. 1, if all the junctional channels are closed, the coupling resistance is infinite; thus, even a 100-mV jump in C_1 evokes no current at all in C_2 . Sometimes a succession of staircase-type events of similar amplitude are seen during one voltage jump (Fig. 3a, b). The simplest interpretation is that the steps represent successive openings of identical channels, although the possibility that they represent different substates of one channel cannot be excluded. During other voltage jumps, non-quantal conductance changes are observed (Fig. 3a, b, d). Thus, the junctional conductance changes with time, but current amplitude histograms indicate clearly that preferential levels of current are reached during the voltage jumps (Fig. 3c). The three discrete peaks at 0, 7.2 and 13.6 pA (Fig. 3b, c) strongly suggest the existence of quantal changes of conductance with a unitary conductance of 110–130 pS. The histograms also show that intermediate levels of conductance are randomly distributed between the peaks. In five different pairs of cells, the conductance measured from the smallest quantal change appearing in similar histograms was in the range 70–180 pS, with an average of 120 pS. We suggest that this is the elementary conductance of a fully open junctional channel. Alternatively it may correspond to the conductance of a group of junctional channels, in which case the true elementary conductance would be considerably less than 120 pS. This seems, however, to be incompatible with experiments (see ref. 2 for review) in which the permeability of intercellular junctions to molecules of various sizes was measured, and from which an elementary conductance of at least 100 pS has been predicted³.

Kinetic peculiarities

Junctional channels between embryonic cells seem to stay open for several seconds^{5,18}. A similar situation was found for the junctional channels of lacrimal cells. For example, in the experiment shown in Fig. 3b, a channel that was open at the onset of a voltage jump was still open at the end of the pulse (0.4 s later) in 20 out of 25 occasions. The channel closing rate was thus of the order of 0.5 s^{-1} , which gives a channel mean open time of 2 s in this experiment.

A more surprising feature was that several tens of milliseconds are generally necessary for a complete transition between two

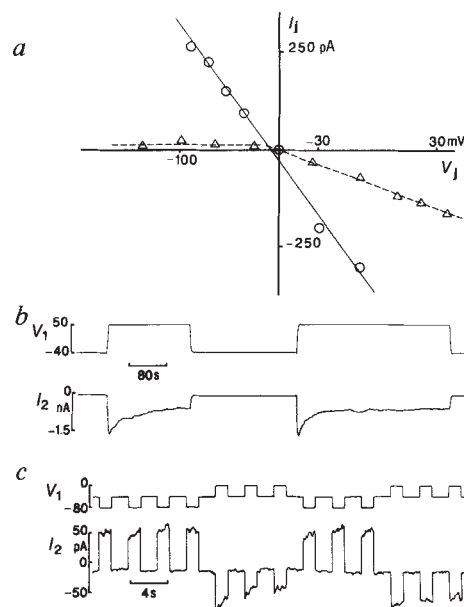
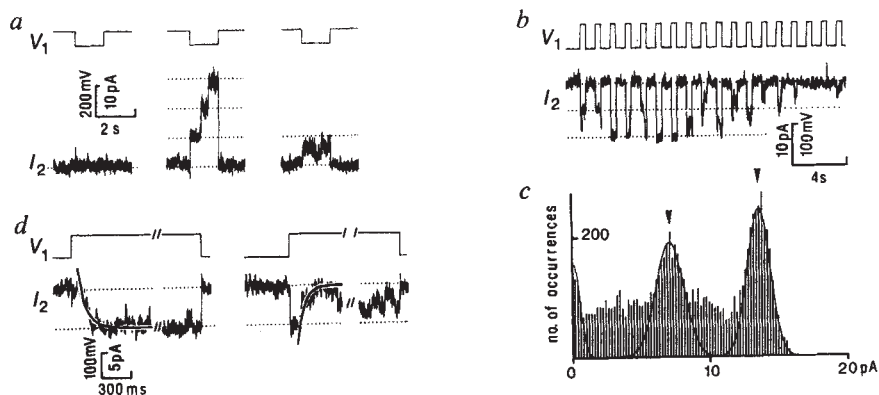


Fig. 2 Voltage dependence of the transjunctional current shown in three different pairs of coupled cells. *a*, Current I_j flowing through a junction as a function of transjunctional potential V_j ; pipettes filled with solution A. The experimental protocol and the corrections are identical to those shown in Fig. 1. The initial I - V curve ($\circ$) gives an initial conductance $G_j = 7.2\text{ nS}$. A linear relation between transjunctional current and transjunctional potential has been observed for a range of holding potentials from -80 to $+10\text{ mV}$. The I - V curve (Δ) was obtained 9 min later, when a partial uncoupling had spontaneously developed. When C_1 was depolarized, G_j had a value of 1.9 nS (currents measured at the end of the voltage pulses). The uncoupling was almost total when C_1 was hyperpolarized. *b*, Current (I_2) measured in C_2 in response to changes in command voltage in C_1 (V_1 was changed from -40 to $+50\text{ mV}$ by hand, not instantaneously); the half-decay times of the two current changes were 37 and 23 s, respectively. This decrease in I_2 is not caused by an artefactual decrease in the transjunctional voltage: the current in C_1 (not shown) presented, like I_2 , a time-dependent decrease. Therefore the transjunctional voltage had slightly increased with time. Pipettes 1 and 2 were filled with solutions A and H, respectively. *c*, Current measured in C_2 in response to repetitive voltage jumps V_1 of $+/-40\text{ mV}$ in C_1 ; pipettes filled with solution A. In this experiment, after the development of a spontaneous partial uncoupling, the junctional conductance increased during the command voltage jumps when C_1 was hyperpolarized (shown) or when C_2 was depolarized (not shown), and decreased in the reverse situation. In *b* and *c*, I_2 became noisy during the V_1 jump. Spectral analysis of the noise was not possible because (see text) the underlying channels have several conductance levels and may not be functionally independent.

quantal levels of conductance. This was observed for conductance changes that took place during the voltage jumps. These conductance changes were always much slower than the current changes observed at both the onset and offset of the voltage jumps (Fig. 3d). A square change of current synchronous with the onset of a voltage jump indicates that a channel was probably open before the jump, but that its open state could not appear in the absence of a transjunctional potential. As expected, the time constant of such a current change ($<1\text{ ms}$) was determined by the low-pass filtering of the recordings, and was 1–2 orders of magnitude briefer than the slow transitions observed during the voltage jumps. To quantify these slow transitions, they were fitted by an exponential which was often (Fig. 3d, left), but not always (Fig. 3d, right), a reasonable description of the observed current changes. The time constant of the exponentials was $53 \pm 48\text{ ms}$ (mean $\pm$ s.d., $n = 15$) for conductance increases, and $118 \pm 79\text{ ms}$ ($n = 15$) for conductance decreases. These slow transitions must reflect either conformational changes or slow blockings and unblockings of the junctional channels. The rate of transition between the open and closed states of ionic channels

Fig. 3 Single junctional channel currents recorded in two different pairs of cells and filtered at 500 Hz. *a, d*, Selected recordings obtained from an almost completely uncoupled pair of cells; pipettes filled with solutions D and E. I_2 changes were induced by repetitive voltage jumps V_1 of 100 mV from a holding potential of -50 mV. *b*, Continuous record of V_1 and I_2 in another almost completely uncoupled pair of cells. Holding potentials -50 mV. Depolarizing pulses V_1 to +10 mV. Pipettes filled with solution A. *c*, Amplitude histogram derived from 29 consecutive I_2 current responses to V_1 voltage pulses including those shown in *b*. Sampling frequency 500 Hz. Every digitized point is counted as one occurrence, and hence the relative heights of the peaks are proportional to the fraction of time spent at the various current levels. The dotted lines in *b* correspond to the two amplitude peaks marked by the arrows in *c*. *d*, Note the change in timescale and polarity of the voltage jumps between *a* and *d*. In *d*, the time constants of the exponential fits, which have been superimposed on the current traces, are 89 ms (left) and 76 ms (right).



studied so far is always very high (for example, $>10^5 \text{ s}^{-1}$ for the acetylcholine-activated channel¹⁹). The actual transition rate from the open to the closed state should not be confused with the rate constant of closure of a channel, which is the inverse of its mean open time. The slow conformational changes that we have observed are thus quite unexpected for a channel protein.

We could be dealing with a succession of several unresolved conformational changes, each very fast. The actual time course would be a series of small staircases and the shape of its envelope determined by the relative heights of the successive energy barriers. If the opening of the junctional channel results from a rearrangement of its subunits²⁰, this process could also be unusually slow. Alternatively, the slow conductance changes may be the result of the movements of a blocking molecule or particle that could even be part of the junctional channel itself^{21,22}. This particle may obstruct one mouth of the channel, or pass through the channel, temporarily reducing its conductance. Either way, it cannot diffuse freely in the cytoplasm because it would then rapidly disappear into the pipette solution.

Concerted openings and closures

On several occasions, the transjunctional current presented abrupt changes much larger than those described above. In the experiments illustrated in Fig. 4, a slight voltage dependence of the junctional conductance was perceptible; when cell 1 was depolarized, the conductance of the junction showed a reversible decrease. In addition, occasional large conductance jumps of $\approx 5,000 \text{ pS}$ were seen (Fig. 4*a, b*). In gap junctions, junctional channels are densely packed and form particle aggregates. The large conductance changes that we have observed could be caused by a cooperative gating of channels in such clusters, leading to a more-or-less synchronous opening or closing of 10–40 channels.

Ionic selectivity

All the conductance measurements described above were made with microelectrodes filled with intracellular solutions A–E, that is, with K^+ and Cl^- as the major charge carriers. To determine the ionic selectivity of the junction, pairs of cells were dialysed with solutions that differed on the two sides of the junction. In this asymmetrical situation and with a strongly coupled pair of cells both kept initially at a holding potential of -50 mV, we could measure the reversal potential of the transjunctional current by simply changing the holding potential in one of the two cells (for example, C_1) until no current flows through the junction. In practice, this was obtained when the current provided by the amplifier connected to the cell C_2 that clamps this cell at -50 mV becomes zero (see Fig. 1 legend). The relative permeabilities of the ions can be then estimated from the value of the reversal potential, using the Goldman equation, and after the liquid junction potentials had been measured in a separate

experiment with a flowing KCl electrode. In a series of experiments, zero current was obtained when cell 1, which contained 140 mM KCl (solution A), was hyperpolarized by $5.6 \pm 1.1 \text{ mV}$ (mean $\pm$ s.d., $n=4$) with respect to cell 2, which was dialysed with a solution containing four times less KCl and 158 mM mannitol (solution I). This gives a permeability ratio $P_{\text{K}}/P_{\text{Cl}} = 1.45$ for junctional channels.

In another series of experiments, with NaCl in one cell (solution H) and KCl in the other (solution A), zero current was obtained when the KCl-dialysed cell was made $3 \pm 1.6 \text{ mV}$ (mean $\pm$ s.d., $n=3$) more negative than the other one. Taking into account the above value of $P_{\text{K}}/P_{\text{Cl}}$, this gives a ratio $P_{\text{K}}/P_{\text{Na}} = 1.23$. By comparing the relative values of P_{K} , P_{Na} and P_{Cl} (1, 0.81 and 0.69) and the relative mobilities of K^+ , Na^+ and Cl^- in water (1, 0.68 and 1.04), it appears that the difference between P_{K} and P_{Na} can be explained qualitatively by the different mobilities of these ions in an aqueous channel. On the other hand, the slightly lower permeability of Cl^- relative to cations might be caused by fixed anionic charges in the channels (see refs 23, 24). Ionic channels that discriminate poorly between cations and anions are not common (but see refs 25, 26). In the case of junctional channels, the absence of selectivity was expected, as it is known that both negatively and positively charged molecules can pass through the junction (see refs 1, 2).

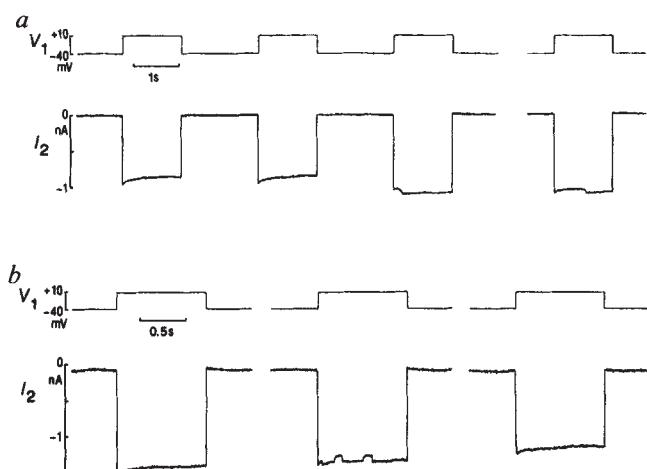


Fig. 4 Concerted transitions of several junctional channels in two cell pairs. In both cases, depolarizing voltage jumps V_1 of 50 mV were applied from a holding potential of -40 mV. *a*, Junctional conductance jumps of 1,500–1,250 pS are seen during the third and fourth voltage jumps. A conductance increase of $\sim 5,000 \text{ pS}$ also occurred between the second and the third voltage pulses. Pipettes filled with solutions A and H. *b*, Conductance jumps of $\sim 2,600 \text{ pS}$, pipettes filled with solutions B and A.

Conclusion

The picture of the junctional channel that emerges from these experiments is of an unusual ionic channel. The fully open channel has a conductance of ~ 120 pS, but states of lower conductance (caused by partial opening or partial obstruction) are frequently encountered. The transitions between the open and closed states are surprisingly slow (several tens of milliseconds). It is conceivable that during these transitions, the channel molecular complex spends some time in several of the states corresponding to the intermediate levels of conductance. The occasional observation of larger conductance jumps suggests that groups of channels operate with a strong internal cooperativity. Finally, the junctional channels discriminate

poorly between cations and anions, cations being slightly more permeable than anions.

The double patch-clamp technique, by enabling control of the composition of the solutions bathing the two faces of a junction, appears to be well suited to the study of mechanisms controlling the permeability of intercellular junctions. For instance, our experimental approach (see also ref. 27) should help to elucidate the intracellular mechanisms involved in the modulation of cell-cell junctions by neurotransmitters²⁷⁻³¹.

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LETTERS TO NATURE

Possible cosmological scenario with an unstable 17-keV neutrino

T. Padmanabhan & M. M. Vasanthi

Tata Institute of Fundamental Research, Homi Bhabha Road, Bombay 400 005, India

changing neutrino current ($\nu_H \rightarrow \nu_L + f$). The lifetime (τ) for such a decay¹⁰ is given by

$$\tau = 6.72 \times 10^{11} \left(\frac{F}{10^{10} \text{ GeV}} \right)^2 \left(\frac{m_H}{17 \text{ keV}} \right)^{-3} \text{ s} \quad (1)$$

where F is the symmetry-breaking scale for the interaction and m_H is the mass of ν_H . From the μ -e decay one can obtain the lower bound

$$F_{10} \equiv \left(\frac{F}{10^{10} \text{ GeV}} \right) \geq 0.14 \quad (2)$$

There are essentially no other constraints on F . We assume that ν_L has a mass in the range $10 \text{ eV} < m_L < 40 \text{ eV}$, as suggested in some experiments¹¹. Most of our results do not depend crucially on the value of m_L .

The cosmological scenario that follows from the above assumptions is easy to analyse¹²⁻¹⁵. At very early epochs, $z \gg 10^{10}$, ν_H remains in equilibrium and decouples at $z \sim 10^{10}$ (ref. 9). (Helium synthesis takes place around this epoch. The effect of ν_H on helium is under investigation.) As the Universe cools, ν_H becomes non-relativistic at the redshift of $z = z_{\text{NR}} \approx 10^8$ (when $kT = m_H c^2$) and begins to dominate the energy density ($\rho(\nu_H) = \rho(\text{others})$), slightly later at $z = z_{\text{eq}} = 5.5 \times 10^6 m_{17}$ (we denote ($m_H/17 \text{ keV}$) as m_{17}). The time elapsed since the big bang is

$$t_{\text{eq}} = 2.97 \times 10^6 m_{17}^{-2} \text{ s} \ll \tau \quad (3)$$

so that the decay of ν_H is completely negligible at these epochs. For $t_{\text{eq}} < t \leq \tau$ the Universe is completely dominated by the non-relativistic ν_H . The expansion factor $S(t)$ varies as $t^{2/3}$ during this epoch. For $t \gg \tau$ the decay of ν_H becomes important. We take the decay to be virtually complete at $t = t_D$ when $\rho(\nu_H) \leq \rho(\text{others})$ again. A simple calculation gives

$$t_D \approx 10.4 \tau \quad (4)$$

The photon temperature at the half-life time is $T_\gamma(\tau) =$

Simpson¹ has recently reported evidence for a heavy neutrino of $\sim 17.1 \text{ keV}$ mass. Cosmological bounds on stable neutrino species imply that this neutrino (ν_H) must be unstable. The most likely decay mode, $\nu_H \rightarrow \nu_L + f$ where ν_L is a light neutrino and f is a scalar boson, leads to the cosmological scenario presented here, which is quite different from the conventional one. In this scenario, the Universe becomes matter dominated at a redshift of $z \sim 10^7$ and becomes radiation-dominated (by the decay product ν_L of ν_H) at $z \sim 310$. The kinematic constraints on the lifetime of ν_H do not lead to any contradictions. On the other hand, the growth of baryonic perturbations is severely limited in this model because virtually no growth can take place in the radiation-dominated region $z < 310$ and decay of ν_H is likely to disrupt and smooth-out past growth by a large factor. It is doubtful whether there is a simple way to avoid this difficulty.

A stable ν_H with a mass of 17 keV will provide the Universe with ~ 300 times the closure density ρ_c (for bounds on neutrino masses from cosmology, see refs 2, 3), which is excluded by the observational bounds on the deceleration parameter (see ref. 4). Among the possible decay channels available, the radiative channel ($\nu_H \rightarrow \nu_L + \text{photons}$) is severely constrained by the photon emissivity of the Galaxy⁵⁻⁸, whereas the decay mode $\nu_H \rightarrow \nu_L \bar{\nu}_L \nu_L$ has a much longer half-life than the age of the Universe⁹. A remaining possibility is the decay of ν_H (identified with muon neutrino) into ν_L (identified with electron neutrino) and a Goldstone boson f that couples weakly to a flavour-

$2.8 \times 10^3 m_{17}^{5/3} F_{10}^{-4/3}$. We consider the decay to have occurred between $t = \tau$ and $t = t_D$.

In conventional scenarios, the Universe would have been dominated by non-relativistic matter (either baryons or massive light neutrinos) at $T_\gamma \approx 3,000$ K. The situation here is different. Every ν_H produces a ν_L with an energy of $\sim 0.5 m_H = 8.5$ keV on its decay. (The f -particle which carries $0.5 m_H$ is virtually massless in most models.) As $m_L < 40$ eV, the electron neutrinos are extremely relativistic at the time of production. Because their number densities are of the same order as that of photons and primordial ν_L , these relativistic decay products dominate the energy density for $t > t_D$. Because most of the ν_H decays at $t \gg \tau$, a reasonable fraction of decay product ν_L will become non-relativistic only when the radiation temperature is lower than

$$T \approx T(\tau) \left(\frac{m_L}{8.5 \text{ keV}} \right) \approx 3.2 \text{ K} \left(\frac{m_L}{10 \text{ eV}} \right) \quad (5)$$

Because the complete evolution of the Universe is known we can compute the age of the Universe to be

$$t_U \approx 4.68 \times 10^{10} F_{10}^{-2/3} m_{17}^{1/3} \text{ yr} \quad (6)$$

Taking the age of the globular clusters $t_{GC} = 1.5 p \times 10^{10}$ yr, where p is the 'personal prejudice factor' ~ 1 , and demand $t_U > t_{GC}$, we obtain the constraint

$$F_{10} \leq 5.51 p^{-3/2} m_{17}^{1/2} \quad (7)$$

A similar constraint can be obtained from the energy density of the decay products of ν_H . This energy density is given by

$$\rho = 2.82 \times 10^{-27} \text{ g cm}^{-3} m_{17} \left(\frac{\tau}{t_U} \right)^{1/2} \quad (8)$$

(It is assumed that $t_0 = \nu_H$ -decoupling epoch $\ll \tau \ll t_U$; see ref. 9.) Demanding $\rho \leq \Omega_m \rho_c$ (where Ω_m is another prejudice factor expected to be ~ 1), we obtain ($H_0 = 100 h_0 \text{ km s}^{-1} \text{ Mpc}^{-1}$)

$$\left(\frac{\tau}{t_U} \right) \leq 4.98 \times 10^{-5} \Omega_m^2 h_0^4 m_{17}^{-2} \quad (9)$$

which, when coupled with equations (1) and (6), produces the constraint

$$F_{10} \leq 2.45 \Omega_m^{3/4} h_0^{3/2} m_{17}^{1/2} \quad (10)$$

Although these are interesting cosmological bounds on F_{10} , they do not lead to any contradiction.

A disturbing contradiction arises, however, when we look at the growth of perturbations in this scenario (see ref. 16). Perturbations in the non-relativistic component cannot grow much in a universe dominated by relativistic particles¹⁷. Thus, the growth of baryonic perturbations is effectively confined to epochs at which $T_\gamma > T_\gamma(t_D)$, that is, $T_\gamma > 590$ K. On the other hand, baryonic perturbations can grow only after they decouple from radiation, that is, only during $T_\gamma < T_{\text{recombination}} \approx 3 \times 10^3$. If one follows adiabatic growth, which evolves as $\propto S(t)$ in the matter-dominated epoch, we obtain a growth factor of only ~ 5 , which is totally insufficient. This argument, however, is not complete. Perturbations in ν_H can grow right from $z \sim 10^7$. There is a possibility that the baryons, as soon as they decouple (at $T \approx 3 \times 10^3$ K) 'fall' into the already existing ν_H potential well and quickly attain a density contrast value of $(\delta\rho/\rho)_B \approx (\delta\rho/\rho)_\nu$ (see ref. 18). It turns out that the values are still insufficient.

From the study of galaxy-galaxy correlation function, it is known that the scales which are entering the nonlinear regime today $(\delta\rho/\rho) \sim 1$ have a size $L \approx 5 h_0^{-1} \text{ Mpc}$. This length scale L entered the horizon in the past (in the ν_H -dominated era) when the radiation temperature was

$$T_L = T(\tau) \left(\frac{3c\tau}{L} \right)^2 \left(\frac{T_\tau}{T_{\gamma_0}} \right)^2 \approx 9.8 \times 10^4 \text{ K} \quad (11)$$

In the best possible situation, the growth factor obtainable (ε) is

$$\varepsilon \equiv \frac{T_L}{T(10.4\tau)} \approx 170 \quad (12)$$

(In equation (12), it is assumed, unrealistically, that the density contrast of baryons instantaneously increases to the pre-existing ν_H -density contrast, just after decoupling.) Thus, the perturbations when they enter the horizon must have an amplitude

$$\left(\frac{\delta\rho}{\rho} \right)_H = \varepsilon^{-1} = 6 \times 10^{-3} \quad (13)$$

which is ~ 600 times higher than the usually accepted value of 10^{-5} . Currently popular models interpret $(\delta\rho/\rho)_H$ to be the signature of quantum fluctuations that 'went out' of horizon at a primordial epoch¹⁹. It is difficult to imagine a scenario that will allow widely different $(\delta\rho/\rho)$ for neutrinos and baryons at the primordial epoch. (The baryonic part of $(\delta\rho/\rho)$ is severely constrained by observations on temperature anisotropies of microwave background to be $\leq 10^{-5}$.) The existence of 17-keV ν_H may thus undo the original benefits of a neutrino-dominated Universe.

There is another problem with the dynamics. When the ν_H decays, all scales at which

$$t_{\text{dyn}} > \tau \quad (14)$$

(where t_{dyn} is the dynamic, free-fall timescale of the particular condensate) will be disrupted. For galactic sizes, $t_{\text{dyn}} \approx 3.15 \times 10^{15} \text{ s}$ and $\tau \approx 10^{12} F_{10}^2 m_{17}^{-3} \text{ s}$. We cannot violate equation (14) while maintaining the bound equation (10) on F_{10} . It is necessary to assume that only scales much smaller than galactic sizes survive the disruption. Stable scales (with $t_{\text{dyn}} < \tau$) will respond adiabatically and increase in size by a factor of $f \sim (\rho_\nu/\rho_B) \sim 10^3$. Still, one would expect larger clustering at small scales than predicted in the standard scenarios.

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HCN emission from OH infrared sources

Shuji Deguchi

Department of Physics, University of Illinois at Urbana-Champaign,
1110 West Green Street, Urbana, Illinois 61801, USA

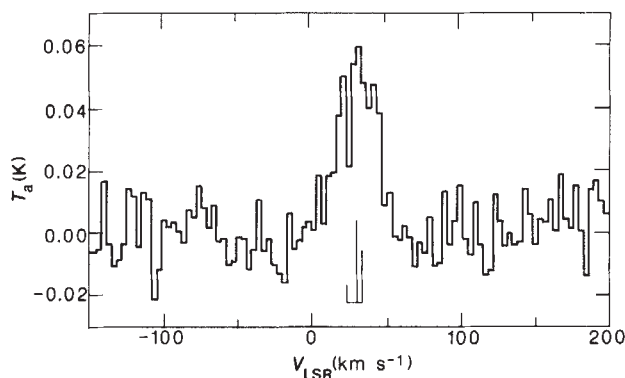
Paul F. Goldsmith

Five College Radio Astronomy Observatory,
University of Massachusetts, Amherst, Massachusetts 01003, USA

Radio line emission of the HCN molecule has been considered to be a tracer of carbon-rich circumstellar environments¹. We report here, however, the detection of HCN radio emission from oxygen-rich late type stars. These results relate to the issue of the progenitors for planetary nebulae². The presence of the HCN molecule in oxygen-rich stars suggests that complex photochemical reactions are proceeding in the outer circumstellar envelope of late type stars.

Table 1 OH/infrared sources with HCN emission

Name	RA (1950.0)	Dec. (1950.0)	T_a (K)	V_{LSR} (km s ⁻¹)	ΔV (FWHM) (km s ⁻¹)	Distance (kpc)
IK Tau (=NML Tau)	3 h 50 min 44 s	11° 15' 30"	0.05	32	36	0.3
OH231.8+4.2 (= OH0739-14)	7 39 59	-14 35 44	0.05	34	28	1.8

**Fig. 1** The HCN $J=1-0$ spectrum of IK Tau taken on 9 March 1985 in the 1-MHz 256-channel filter bank. The hyperfine splitting is shown.

We observed 14 OH/infrared sources in the $J=1-0$ transition of HCN and detected weak HCN emission in two sources: IK Tau and OH 231.8+4.2. These observations of HCN at 88.6 GHz were performed at the Five College Radio Astronomy Observatory with the 14-m radio telescope in December 1981, February 1985 and March 1985 using a cooled 3-mm receiver and 1 MHz $\times$ 256 channel and 0.5 MHz $\times$ 256 channel filter banks. The system temperature was ~ 400 – 600 K. The half-power beam width is ~ 60 arcs at 88 GHz and the aperture efficiency is ~ 0.40 . The observational results are summarized in Table 1.

In Fig. 1, we present the HCN spectrum of IK Tau. The line profile seems to be parabolic, although noise and an overlap of hyperfine components significantly deform the original line shape. The absence of a flat top to the line profile is usually interpreted to indicate that the HCN line is optically thick in the expanding circumstellar envelope of IK Tau (ref. 3). The OH, H₂O and SiO maser emissions have been detected in this source⁴, and the thermal emission of the CO $J=1-0$ transition has also been detected⁵. The radial velocity and the linewidth of the HCN emission agree well with those of the maser and thermal emission lines of this star.

The bipolar reflection nebula, OH231.8+4.2, is an unusual OH/infrared source⁶. Emissions by H₂O, SiO and H₂S have been detected⁷⁻⁹. The HCN emission from this source was at first detected from the upper side band of the receiver during the ²⁹SiO $J=2-1$ maser search¹⁰ on 25 December 1981. Subsequent observations have shown that the emission profile agrees well with the SiO and H₂S profiles in radial velocity and width. To confirm that the HCN emission is associated with the star, we obtained the spectrum at a position 2 arc min north of the source and at another position 6 arc min south-west which coincides with the planetary nebula NGC2438 (refs 11, 12). No emission above 0.03 K (r.m.s.) was detected. The HCN emission from OH231.8+4.2 was also detected recently in independent observations by P. R. Jewell (personal communication).

In addition to the above two sources, we have detected a narrow HCN emission line in the direction of OH/infrared source OH32.8-0.3 ($T_a \sim 0.1$ K at $V_{LSR} = 86$ km s⁻¹). It does not agree in radial velocity with the OH 1,612-MHz double peaks of OH32.8-0.3 ($V_{LSR} = 46$ and 76 km s⁻¹)^{13,14}. This narrow line is probably not associated with the star, but with a molecular cloud in this direction. The narrow width ($\Delta V \sim 4$ km s⁻¹) of the line and the presence of the background (or foreground)

CO cloud in this direction¹⁵ ($V_{LSR} \sim 90$ km s⁻¹ at $l = 33^\circ$ and $b = -0.4^\circ$) support this idea.

The late type stars with mass loss rate as high as $10^{-4} M_\odot$ yr⁻¹, such as carbon stars, have been considered as progenitors of planetary nebulae. The HCN radio emission has been observed in the circumstellar envelope of carbon stars¹. In an oxygen-rich environment, all carbon atoms are expected in chemical equilibrium consideration to be incorporated into molecular CO, so that negligible C-compounds other than CO should be present^{16,17}. The detection of HCN molecules in apparently oxygen-rich circumstellar envelopes like IK Tau and OH231.8+4.2, therefore, provides several implications. First, chemical reactions are proceeding in the outer circumstellar envelope due to the photodissociation of CO molecules. The idea that the OH molecules are produced in OH/infrared sources by dissociation of H₂O caused by the interstellar ultraviolet radiation at radii 10^{16} to $\sim 10^{17}$ cm is generally accepted^{18,19}. Self-shielding would be important for CO molecules so that the dissociation of CO occurs well outside the H₂O dissociation region²⁰. The photodissociation timescale is of the order of 10^4 yr, comparable to the expansion timescale of the circumstellar envelope. The photochemistry of this CO dissociation region is a tempting explanation for this HCN emission in oxygen-rich circumstellar envelopes. Another possibility is that the outer circumstellar envelope of these stars is carbon-rich. This hypothesis requires a source of carbon-rich material, which might, for example, be a carbon-rich star as a binary counterpart of the OH/infrared source. The carbon-rich material may surround the OH/infrared source in the form of a disk. However, broad linewidths of the HCN emission in IK Tau and OH231.8+4.2 suggest that the HCN molecules exist in the same region as the oxygen-rich outflowing envelope, which questions this interpretation.

The other implication of the detection of HCN in OH/infrared source is in relation to the origin of the 3.08- μ m band at near infrared wavelengths. In oxygen-rich stars, this band has been interpreted as caused by the absorption by water-ice grains²¹. Because the same band is present in infrared spectra of carbon stars²², it is suspected that the 3.08- μ m band in OH231.8+4.2 (ref. 23) is due to the vibrational band of polyatomic molecules, that is, the ν_1 band of HCN or the ν_3 band of C₂H₂ (ref. 24). The 3.08- μ m band is also found in the infrared spectrum of OH32.8-0.3 (ref. 25). Our detection of the HCN molecule in these stars implies that the molecular band hypothesis for the origin of 3.08- μ m band cannot be excluded simply because of the oxygen richness of these stars. A detailed comparison of the observational band shape with a laboratory spectrum must be made. Note that HCN emission was detected²⁶ in the direction of HD29647 where the 3.08- μ m band was also observed²⁷. Here the phenomenon is presumably of interstellar origin.

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Table 1 Solar velocity (km s^{-1}) perpendicular to the galactic plane with respect to local interstellar material and young stars

Interstellar material			Young stars		
Objects	$Z_{\odot}$	Ref.	Objects	$Z_{\odot}$	Ref.
H I clouds	7.7	15	OB stars	6.3*	23
	8.5	16		6.9	24
	8.8	17		7.2*	25
	9.4	18		7.3*	26
	11.2	19		7.5*	12
Ca II clouds	12.1*	20		7.7	27
	9.3	22		7.8	28
				9.1	22
			Classical Cepheids	6.4	29
Molecular clouds	11.4*	12		7.3	30
	—			8.2	31
	—			10.0	32
	—			11.4	33
Gas and dust (mean)	9.6		Stars (mean)	7.9	

Solar motion solutions were based on observed radial velocities for the interstellar material and on observed radial velocities and proper motions for the young stars.

* An average of published solutions has been taken. For the O and B stars, only solutions for stars with distances $r \leq 1.3$ kpc have been used in forming the averages.

because the Sun moves through this region very quickly, so $z_{\odot} = 10 \pm 10$ pc will be adopted.

$Z_{\odot}$ is probably indistinguishable from the z component of the Sun's motion with respect to the local standard of rest (LSR). The LSR is most accurately determined from velocity observations of the local gas, dust and young stars, because these objects suffer relatively little selection bias in surveys, while they possess a strong concentration towards the galactic plane, have low random velocities with little or no systematic drift motion perpendicular to the galactic plane (either observationally¹² or theoretically^{13,14}), and contribute a significant fraction of the local mass density⁴. Recently published values of $Z_{\odot}$ are listed in Table 1 (refs 12, 15–33). The apparent difference of 1.7 km s^{-1} between the mean values of $Z_{\odot}$ for young stars and diffuse matter probably has no significance because the ranges of $Z_{\odot}$ within the two groups of objects are very similar. All 22 values listed in Table 1 yield $\langle Z_{\odot} \rangle = 8.6 \pm 1 \text{ km s}^{-1}$ (estimated mean error). This exceeds by a moderate amount the commonly quoted estimates of $6\text{--}8 \text{ km s}^{-1}$ (refs 8, 34, 35) which, although heavily weighted (40–100%) by young stars and diffuse matter, are based on data >25 yr old.

The vertical concentration of objects in the flat galactic subsystem can be determined by measuring their mean absolute height $\langle |z| \rangle$, r.m.s. height $\langle z^2 \rangle^{1/2}$, exponential scale height β , or gaussian dispersion σ , where β and σ are defined by

$$N(z) = N_0 \exp(-|z|/\beta) \quad (3)$$

and

$$N(z) = N_0 \exp(-z^2/2\sigma^2) \quad (4)$$

An exact exponential distribution will have $\beta = \langle |z| \rangle$ and $\langle z^2 \rangle^{1/2}/\langle |z| \rangle = 1.41$, whereas an exact gaussian distribution will have $\sigma = \langle z^2 \rangle^{1/2}$ and $\langle z^2 \rangle^{1/2}/\langle |z| \rangle = 1.25$. The gaussian half-width at half-maximum is $z_{1/2} = 1.18\sigma$.

Table 2 contains empirically determined values of $\langle |z| \rangle$, $\langle z^2 \rangle^{1/2}$, β and σ , adopted from 14 recently published studies for the solar neighbourhood^{5,9,10,36–46}. All values that depended on kinematical distances obtained by the method of circular galactic rotation have been adjusted to fit a best-estimate solar galactocentric radius of $R_0 = 8.5 \pm 0.5$ kpc (refs 47, 48). Of necessity, classical Cepheids and H I clouds have been omitted from consideration because they exhibit a wider dispersion than do

Terrestrial record of the Solar System's oscillation about the galactic plane

Richard B. Stothers

National Aeronautics and Space Administration,
Goddard Space Flight Center, Institute for Space Studies,
2880 Broadway, New York, New York 10025, USA

Impact cratering on the Earth over the past 600 Myr has been partly sporadic, partly episodic. The episodic component is suspected to have been cyclical, with a mean period of ~ 32 Myr (refs 1, 2). According to a theory proposed to explain this phenomenon¹, gravitational encounters between the Solar System and interstellar clouds of intermediate to large size occasionally disturb the outer Solar System comets, with the consequence that some of these comets fall into the inner regions of the system, where a few hit the Earth. Because the episodes of impact cratering, however, are not precisely periodic^{1,3}, the galactic mechanism must be in part stochastic. The irregular part can be attributed to the randomness in the local space distribution of the interstellar clouds (and various other perturbing galactic objects⁴). The periodic component probably arises from the harmonic oscillation of the Sun about the galactic plane, since the large-scale space density of the interstellar clouds and other objects falls off with increasing distance from the plane. A new study of the observational evidence is presented here. Contrary to a claim by Thaddeus and Chanan⁵, the vertical scale height of the clouds seems to be sufficiently small and the Sun's vertical trajectory sufficiently large for the modulating effect of the Sun's galactoververtical motion to be detectable in the terrestrial record of impact cratering with at least a 50% *a priori* probability.

The Sun's past oscillations perpendicular to the galactic plane have probably always been confined within $|z| < 300$ pc, and so they have probably closely followed simple harmonic motion⁶. The present vertical amplitude, z_{max} , can be determined from the Sun's present height, $z_{\odot}$, its present velocity, $Z_{\odot}$, and the half-period of oscillation, $P_{1/2}$, by means of the relation

$$z_{\text{max}} = (z_{\odot}^2 + P_{1/2}^2 Z_{\odot}^2 / \pi^2)^{1/2} \quad (1)$$

The half-period (that is, the time elapsed between successive crossings of the galactic plane) follows from Poisson's equation as⁶

$$P_{1/2} = (\pi/4G\rho_0)^{1/2} \quad (2)$$

where ρ_0 is the local mass density in the galactic plane and G is the gravitational constant.

The Sun's height above the Galaxy's mean plane is usually taken to be $z_{\odot} = 8 \pm 12$ pc from H I observations^{7,8}. Molecular cloud observations confirm that $z_{\odot} \approx 0$ (ref. 9), but the observed distribution of young stars and star clusters puts the Sun at $z_{\odot} = 20\text{--}30$ pc (refs 7, 10, 11). The exact value of $z_{\odot}$ is not critical

Table 2 Characteristic galactic heights (pc) of local interstellar material and young stars

Object	$\langle z \rangle$	$\langle z^2 \rangle^{1/2}$	β	σ	Ref.
H II regions	62	84	—	—	36
	—	85*	—	—	37
Molecular clouds	—	—	—	42*	38
	—	>53*	—	—	39
	—	—	—	54*	9
	—	—	—	61*	5
OB stars	—	—	—	45	40
	45	—	—	—	41
	50	—	—	—	42
	50	74	46	48	10
	54	—	—	—	43
	54	—	—	—	44
	57	82	—	—	36
Young star clusters	47	65	—	—	36
	53	—	—	—	45
	—	75	—	—	46
	63	79	68	61	10
Gas and dust (mean)	(62)	84	—	52	
Stars (mean)	53	75	57	51	

* Scaled to a solar galactocentric radius of $R_0 = 8.5$ pc.

the other objects. Since the young stars show $\beta/\langle |z| \rangle = 57/53 = 1.08$ and $\langle z^2 \rangle^{1/2}/\langle |z| \rangle = 75/53 = 1.42$, an exponential distribution characterizes them very well. In the case of molecular clouds, values for σ alone have been published. However, as molecular clouds and young stars have formally nearly the same values of σ , it is reasonable to assume that both classes of objects (which are also genetically related) follow the same exponential distribution, at least in the solar neighbourhood where distances are well determined.

Potential sources of observational bias for the various objects used include: heavy interstellar obscuration (of the stars) near the galactic plane, accidental errors in the distances, and warping of the galactic plane. These effects tend to widen the apparent vertical distribution of the objects. Estimates of the actual amount of bias, however, have shown that it is very small^{9,36}; the zero point error in the distances is probably also small⁴⁸. A statistically corrected value of $\beta = 50 \pm 5$ pc will therefore be adopted.

$P_{1/2}$ can be determined from equation (2) through a knowledge of ρ_0 . Direct counts of stars, gas and dust yield $\rho_0 = 0.10$ – $0.11 M_\odot \text{ pc}^{-3}$ (refs 49, 50). Dynamical analyses of stellar motions perpendicular to the galactic plane have produced best-estimate values covering the range 0.075 – $0.235 M_\odot \text{ pc}^{-3}$ (14 values are listed by Krisciunas⁵¹ and seven values come from other sources^{49,50,52–56}). The mean of all 21 dynamically determined values is $0.145 \pm 0.01 M_\odot \text{ pc}^{-3}$. However, the latest dynamical studies by Bahcall⁵⁰ have produced a modern series of allowed values covering the range 0.10 – $0.35 M_\odot \text{ pc}^{-3}$, his best estimate being $0.185 \pm 0.02 M_\odot \text{ pc}^{-3}$. I shall therefore adopt $0.18 \pm 0.04 M_\odot \text{ pc}^{-3}$. This corresponds to $P_{1/2} = 31 \pm 3$ Myr and implies that almost half of the local matter is invisible.

Using the above results for z_0 , Z_0 and $P_{1/2}$, equation (1) yields $z_{\max} = 88 \pm 13$ pc. Consequently, $z_{\max}/\beta$ must be 1.8 ± 0.3 , which is not significantly different from Rampino and Stothers's¹ assumed value of 1.6.

The Sun's orbital revolution around the galactic centre probably has had little direct effect on $z_{\max}/\beta$. At present, the Sun lies very near the pericentre of its orbit, unless encounters with the most massive interstellar clouds and the Galaxy's spiral arms have significantly deflected its ballistic trajectory. If the LSR is taken to be also the local rotational standard of rest, the Sun passed the apocentre at $R \approx 1.14 R_0$ (ref. 57). If, however, the LSR is moving outwards from the centre of the Galaxy at $\sim 7 \text{ km s}^{-1}$ (refs 58–61), the Sun's true orbit would be more nearly circular. Over short radial distances beyond the solar circle, β increases as $R^{1.5}$ according to published data compiled for OB

stars, young star clusters and H II regions³⁶, but as $R^{0.5}$ according to published molecular cloud data^{5,9}. Since ρ_0 decreases outward as $R^{-4 \pm 2}$, in typical models of the Galaxy that reproduce the observed surface-brightness distributions and rotation curves of galaxies that are morphologically similar to our Galaxy^{62–65}, $P_{1/2}$ probably increases outwards as $R^{2 \pm 1}$. Azimuthal variations in ρ_0 (refs 9, 39, 66, 67) and secular changes in β over the past 10^9 yr (ref. 68) appear to be small near the solar circle. Therefore, the part of $z_{\max}/\beta$ that is independent of Z_0 probably increases by $< \sim 15\%$ between the pericentre and apocentre of the Sun's orbit. As $P_{1/2}$ over the same range of distance probably increases by 0–30%, the time average of $P_{1/2}$ must have been close to 33 ± 3 Myr.

The Sun's average z velocity during the past 600 Myr is usually assumed to be constant. Note, however, that a close encounter of the Sun with a giant molecular cloud, although expected to be a very rare occurrence^{69,70}, could have significantly deflected the Sun's ballistic trajectory. The Sun's present r.m.s. z velocity averaged over a vertical orbit is $8.6/\sqrt{2} = 6.1 \text{ km s}^{-1}$, which lies well below the ensemble mean for other solar-type stars, $\sim 20 \text{ km s}^{-1}$ (ref. 71). A value of 20 km s^{-1} would produce $z_{\max} \sim 300$ pc and $z_{\max}/\beta \sim 6$. However, I shall adopt in the following calculations $z_{\max}/\beta = 1.8$, as derived above for the unperturbed Sun.

Under the simplest assumptions, the rate at which the Sun encounters known as well as unknown objects belonging to the Galaxy's flat component will be proportional to f_0 , the mass fraction of all flat-component material at $z = 0$ (ref. 4). Observations suggest that f_0 may be as low as 0.17 (and possibly even lower) or as high as 0.75. The largest known contributor to f_0 is interstellar clouds^{9,50}. An improved assumption in this situation is obviously to set the rate of encounters proportional to the relative perturbing influence of interstellar clouds (compared with other galactic objects) on the Sun's halo of comets. However, an 'effective' fraction f of this kind is much harder to estimate than f_0 , although obviously $f > f_0$, since the partial breakdown of the impulse approximation for a close encounter between an interstellar cloud and the Sun's cometary system implies an enhanced gravitational perturbation^{70,72–74}.

The rate of solar encounters with interstellar clouds will also depend on the relative velocity of the encounter. The component of the Sun's peculiar velocity that lies in the direction parallel to the galactic plane is $\sim 20 \text{ km s}^{-1}$, and so the Sun's peculiar velocity is expected to change over a vertical orbit by only $\sim 10\%$, an amount which can be neglected. Therefore, the rate r_i of solar encounters with objects having a scale height β_i and an effective fractional mass density in the plane f_i can be taken to be^{1,4}

$$r_i = C f_i \exp [-(z_{\max}/\beta_i) \sin(\pi\phi)] \quad (5)$$

where $\phi = t/P_{1/2}$ and C is the constant part of the encounter cross-section. Over a vertical orbit, the fraction of encounters that occur in the phase interval ϕ_1 – ϕ_2 is then

$$n/N = \sum_i \int_{\phi_1}^{\phi_2} r_i d\phi / \sum_i \int_0^1 r_i d\phi \quad (6)$$

For simplicity, a two-component galactic model will be adopted, consisting of a flat component with $f_1 = f$ and $\beta_1 = \beta$, and a dispersed component with $f_2 = 1 - f$ and $\beta_2 \gg z_{\max}$. In the following calculations, a fixed phase interval $\phi_1 = 0.25$ to $\phi_2 = 0.75$ will be used, corresponding to the half of the Sun's time that is spent farthest from the galactic plane. Figure 1 shows the numerical results for different values of f and $z_{\max}/\beta$.

Unless f is rather large, the expected proportion of encounters far from the galactic plane will not differ significantly from 0.5. Terrestrial evidence suggests that ~ 20 important encounters have occurred during the past 600 Myr (ref. 2). With $z_{\max}/\beta = 1.8$ and $f \sim 1$, an average of 6 encounters out of a total of 20 are expected to have occurred when the Sun was farthest from the galactic plane. On the basis of the binomial distribution, the probability of obtaining $n/N \leq 0.3$ as the outcome of $N = 20$ Bernoulli trials with individual success probability $p = 0.5$ is

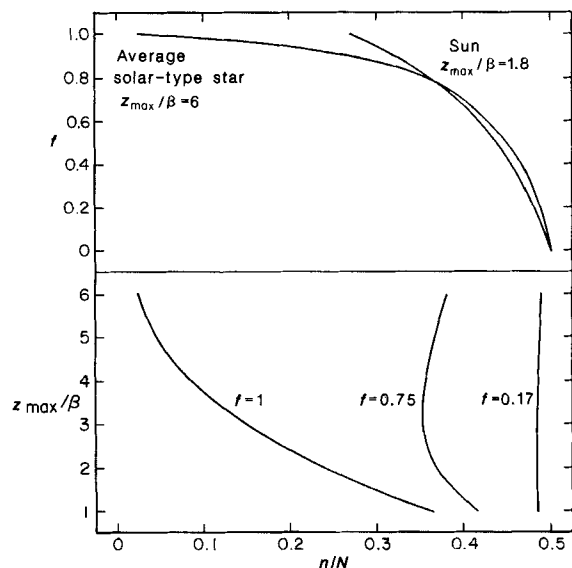


Fig. 1 Expected fraction of the encounters that occur when the Sun is farthest from the galactic plane. This fraction, n/N , is shown separately for the galactic parameters f and $z_{\max}/\beta$.

$P = 0.06$. This suggests that f probably has to exceed f_0 for the galactic model to be viable.

To test this hypothesis in a way that also reduces the many assignable parameters to one, the quantity n/N will be specified. This simplification will not significantly bias the statistical outcome of a large number of Monte-Carlo simulations of the galactic effect if the number of simulations is great enough (tests show that this number must be >20). In each simulation, a pseudo-random time series containing N times drawn at random from a time interval $t = 0$ to $t = T$ will be generated with the constraint that n times randomly occupy a broken subseries consisting of alternate sections of length $P_{1/2}/2$ while $N - n$ times randomly occupy the subseries that is complementary to the first. The complete time series will be formally searched for significant periods in the same way that was used for the observed time series, by computing a power spectrum for a range of trial periods and then picking out the highest spectral peaks². In effect, the theoretical problem has been reduced to specifying the three dimensionless quantities n/N , N and $T/P_{1/2}$, the last being the total number of assumed underlying cycles. In what follows, an explicit value of $P_{1/2} = 33$ Myr, with trial periods of 16–100 Myr, will be adopted. Two typical cases, $N = 10$ for $t = 0$ –297 Myr and $N = 20$ for $t = 0$ –594 Myr, will be considered, while, for each assigned value of n/N , 40 Monte-Carlo simulations will be made.

Figure 2 shows the results, presented in terms of the percentage of the synthesized spectra at each value of n/N that display the highest peak, or one of the two highest peaks, or one of the three highest peaks at a period of $P = 33 \pm 3$ Myr. Spectra that have already been generated for the observed time series of impact craters (and also of geological tectonic phenomena that might be related to impacts) indicate that a significant period of 33 ± 3 Myr usually shows up as the first or second highest peak². Among the synthetic spectra with the observationally favoured value of $n/N = 0.3$, a signal this strong appears in 50% of the spectra for $N = 20$. (The *a posteriori* probability of detection, of course, can be much higher².) Tests with periodic time series show that dephasing of a cycle by artificially introducing noise (corresponding to, say, a deflecting encounter of the Sun with a giant molecular cloud) makes only a few per cent difference in the derived best period and best value of the most recent epoch; even several abrupt phase shifts can be safely tolerated.

In an independent investigation of the galactic model, Thaddeus and Chanan⁵ applied standard Fourier analysis to many comparable pseudo-random time series. They adopted a gaussian z distribution for the flat component (molecular

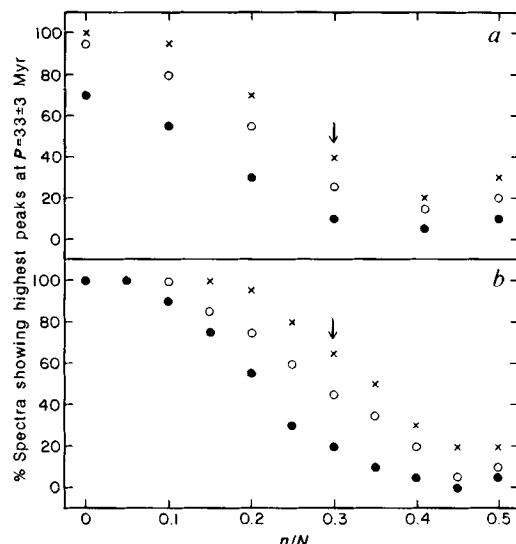


Fig. 2 Percentage of the synthetic power spectra that show one of the three highest peaks at a period of 33 ± 3 Myr. ●, Highest peak alone; ○, the first or second highest peak; ×, case of the first, second or third highest peak. The parameter n/N is the fraction of the encounters that occur when the Sun is farthest from the galactic plane. A small dip in the derived percentages between $n/N = 0.4$ and 0.5 is due to a random statistical fluctuation. a, $N = 10$; $t = 0$ –297 Myr. b, $N = 20$; $t = 0$ –594 Myr.

clouds) and used $z_{\max}/z_{1/2} = 72/85 = 0.85$, thus obtaining a signal-to-noise ratio of 0.45 for $N = 9$. Their adopted value of $z_{1/2} = 85$ pc was based on $R_0 = 10$ kpc (making $z_{1/2}$ too large by 15%) and was weighted heavily by a flare of molecular material out of the galactic plane in the Carina spiral arm. This flare is seen also in OB stars, which, outside the flare and close to the solar circle, show $\langle |z| \rangle = 38$ pc (ref. 75), corresponding to only $z_{1/2} = 56$ pc if a gaussian distribution is assumed. Thaddeus and Chanan also adopted $z_{\max} = 72$ pc, which was based on a value of $Z_0 = 7.4$ km s⁻¹ (refs 8, 35, 76) derived from data now over 25 yr old. By taking averages of more recent data obtained by many different authors and thus reducing the effect of accidental errors, the present analysis of the observational material suggests that $z_{\max}/z_{1/2} = 88/60 = 1.5$. This yields a signal-to-noise ratio of 1.5 for $N = 20$, according to supplementary calculations presented by Thaddeus and Chanan⁵. Although this may still not be detectable with their method, the method that I have used above is demonstrably successful.

The present method of statistical analysis suggests that a galactic signal is potentially detectable (with a 50% *a priori* probability for detection) in the 600-Myr terrestrial time series if the basic model is accepted as now formulated and the following conditions are met: First, ρ_0 must equal $\sim 0.2 M_\odot \text{pc}^{-3}$ to explain the ~ 32 -Myr terrestrial periodicity. This value of ρ_0 accords with the best astronomical evidence and implies that about half of the matter in the galactic disk near the solar circle is unseen. Second, the Solar System's vertical orbit must reach far enough above and below the galactic plane to outdistance most of the matter that is most significantly perturbing the Sun's halo of comets. A value of $z_{\max}/\beta = 1.8$ appears observationally likely. Third, the main perturbing objects as well as the dominant contributors to the mass in the galactic disk (which may not be the same objects) must more or less uniformly populate both the spiral arms and the inter-arm regions to ensure a stable periodicity as the Sun orbits the galactic centre. (Some density enhancement of the perturbing matter in the major spiral arms, however, is possible and may explain the observed ~ 260 -Myr terrestrial periodicity².) Finally, the 'effective' gravitational mass density of the main perturbing objects must exceed their formal spatial mass density in comparison with objects in the dispersed component. Interstellar clouds with intermediate to large masses are likely to be the most important perturbers. It is, therefore, reasonable to conclude that the proposed¹ galactic model of

terrestrial catastrophism is still viable and can be observationally and theoretically tested in various ways.

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Note added in proof: Bahcall and Bahcall⁷⁷ recently studied the Sun's z motion in the framework of a more sophisticated galactic model. They confirmed the approximate validity of the harmonic oscillator model adopted here and by Thaddeus and Chanan⁵. For their applications, however, they used values of $Z_{\odot}$ that are smaller than the best estimate derived here.

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Concordant 3,676 Myr U–Pb formation age for the Kodaikanal iron meteorite

C. Göpel, G. Manhes & C. J. Allègre

Laboratoire de Géochimie et Cosmochimie, Institut de Physique du Globe de Paris et Département des Sciences de la Terre, Universités de Paris VI et VII, 4, Place Jussieu, 75230 Paris Cedex 05, France

The Kodaikanal iron meteorite contains evidence of intensive chemical activity which, according to Rb–Sr studies¹, occurred ~800 Myr after the formation of the Solar System. Here we report the results of U–Pb isotope analyses on a silicate inclusion from Kodaikanal. Leaching experiments on the two major phases, clinopyroxene (CPX) and alkali-rich glass, indicate a contamination by terrestrial Pb attributable to previous curatorial cutting of this iron meteorite. The leached minerals define concordant U–Pb ages that validate the precise Pb–Pb age of $3,676 \pm 3$ Myr. These data are consistent with Rb–Sr age determinations¹. The absence of initial Pb indicates a fast cooling of the silicate material. This has already been established for the metal phase, and a collisional origin for Kodaikanal is favoured.

Kodaikanal is the first iron meteorite with silicate inclusions in which K-feldspar was observed^{2,3}. Rb–Sr isotope analyses of these inclusions show that different mineral fractions and separate inclusions are highly enriched in alkalis and that they lie on one isochron, defining an age of $3,800 \pm 100$ Myr ($\lambda_{\text{Rb}} = 1.39 \times 10^{-11} \text{ yr}^{-1}$) with an initial $^{87}\text{Sr}/^{86}\text{Sr}$ ratio of 0.71 ± 0.02 (ref. 1). This study revealed that the observed age is not simply the result of reheating and reworking of material which had been originally formed at 4,500 Myr, but that it represents silicate formation by chemical differentiation from a reservoir with a much lower (possibly chondritic) Rb/Sr ratio. This study pointed out the occurrence of intensive chemical activity in/on a small planetary body at a time far beyond the early formation of solid objects in the Solar System. Two alternative energy sources which support this late chemical process were proposed: thermal energy stored in a planetary body of 200–500 km radius or kinetic energy dissipated as heat during a collision at 3,800 Myr. Rare gas studies indicate a K–Ar age of $3,500 \pm 100$ Myr for two silicate inclusions⁴ and an exposure age for the Kodaikanal meteorite of 10–20 Myr (ref. 5), which is rather short compared with other iron meteorites. Chemical and mineralogical studies^{6,7} specify the formation of the Kodaikanal material as a mixture of silicates and metal which formed independently. The high degree of chemical and mineralogical fractionation of the inclusions seems to contradict a core origin⁸ but could be explained in a model where differentiated stony material is taken up by an iron melt which was produced in the near crustal portion of a parent body. This mixing event includes: (1) equilibration of the silicates at high temperature and low pressure; (2) fast dispersion of the silicates in the metal phase, which is melted or highly plastic; (3) rapid chilling of the mixture; and (4) subsequent intense deformation. This favours a collisional origin for the Kodaikanal meteorite.

The purpose of our U–Pb study of Kodaikanal was to evaluate the usefulness of this method for dating silicate inclusions of iron meteorites and to help establish the chemical signature of the 3,800-Myr event.

We restricted our study to a single inclusion given the large number of preliminary analyses which are necessary during sample preparation. The inclusion originates from Kodaikanal slice number 1159 from the Paris Natural History Museum (P2 in ref. 6).

The inclusion, which was visible at the surface, was extracted with a tungsten carbide chisel. The two major phases, clinopyroxene (20 vol. %) and alkali-rich glass (80 vol. %) were separated with tweezers under a binocular microscope. To evaluate and to eliminate Pb contamination, the clinopyroxene fraction CPX (7.6 mg) and the glass fraction which was divided in two aliquots, GL1 (11.0 mg) and GL2 (6.6 mg) were leached

Table 1 Pb isotope compositions and Pb-U contents determined in the leachates and in the leached mineral phases

Pb (p.p.b.)	Blank	U (p.p.b.)	Blank	$\frac{^{238}\text{U}}{^{204}\text{Pb}}$	$\frac{^{206}\text{Pb}}{^{204}\text{Pb}}$	$\frac{^{207}\text{Pb}}{^{204}\text{Pb}}$	$\frac{^{208}\text{Pb}}{^{204}\text{Pb}}$	$\frac{^{207}\text{Pb}}{^{206}\text{Pb}}$	$\frac{^{208}\text{Pb}}{^{206}\text{Pb}}$	$\rho(\alpha, \beta)$	$\rho(\alpha, \gamma)$	
Leachates of CPX (7.6 mg)												
l1	864	0.3	1.18	1.1	0.085 ± 13	17.91 ± 22	15.66 ± 18	37.78 ± 44	0.874 ± 5	2.109 ± 10	0.906	0.926
w1	1,776	—	2.19	—	0.078	17.7 ± 4	15.7 ± 4	37.4 ± 1	0.889	2.117		
Leachates of GL1 (11.0 mg)												
l1	424	0.4	4.71	0.2	0.71 ± 6	18.35 ± 2	15.70 ± 2	38.57 ± 6	0.8555 ± 4	2.1014 ± 15	0.927	0.917
w1	725	—	7.20	—	0.83	18.2 ± 2	15.7 ± 2	37.4 ± 3	0.861	2.105		
Leachates of GL2 (6.6 mg)												
l(1-3)	496	0.7	4.21	0.4	0.53 ± 1	17.78 ± 7	15.48 ± 5	38.28 ± 12	0.871 ± 2	2.154 ± 6	0.563	0.683
w1	1,147	—	9.21	—	0.51	18.2 ± 2	15.6 ± 2	38.4 ± 2	0.857	2.111		
CPX (5.8 mg)												
a	19.8	24	0.53	22	1.68 ± 19	18.50 ± 24	15.92 ± 19	37.91 ± 44	0.861 ± 4	2.049 ± 7	0.928	0.967
b	24.5	0	0.64	0	1.65 ± 5	18.38 ± 19	15.86 ± 15	37.87 ± 35	0.863 ± 3	2.061 ± 6	0.928	0.968
c	1,796	—	2.72	—	0.1	17.7	15.7	37.4	0.888	2.116		
GL1 (9.9 mg)												
a	166	8	89.5	0.1	71.9 ± 1.5	150.00 ± 77	60.97 ± 31	157.12 ± 84	0.4065 ± 4	1.047 ± 9	0.985	0.989
b	169	0	89.6	0	58.8 ± 1.3	139.81 ± 70	57.47 ± 29	147.91 ± 29	0.4111 ± 4	1.057 ± 8	0.985	0.989
c	891	—	96.7	—	10.5	25.6	18.2	45.0	0.712	1.759		
GL2 (5.5 mg)												
a	138	2.48	89.9	0.1	993 ± 24	779 ± 15	276.7 ± 5.2	712 ± 14	0.3553 ± 6	0.9141 ± 13	0.997	0.997
b	152	0	90.0	0	285.6 ± 2.3	236.5 ± 2	90.64 ± 76	231.4 ± 2.0	0.3832 ± 4	0.9784 ± 10	0.992	0.993
c	1,285	—	99.2	—	5.4	22.0	16.9	41.8	0.768	1.899		

The sample was leached for 2 min under ultrasonics with 0.2 cm^3 reagent at room temperature. In the case of CPX and GL1, 0.5 M HBr was used for the first 22 steps and 2 M HBr for the last 24 steps; in the case of GL2, H_2O was used for the first 53 steps and 0.5 M HBr for the last 92 steps. The leachate was isolated from the sample and spiked with a ^{205}Pb - ^{233}U tracer, either individually or after regrouping 3–20 successive leachates. After a series of leachings the samples were rinsed with water and stored in a closed beaker. U and Pb were isolated following the procedure described in refs 11, 14. Lines l1 refer to the first leachate, lines w1 to all the leachates which were recalculated from the individual measurements. The values are corrected for experimental effects: (1), mass discrimination ($0.1 \pm 0.03\%$ per atomic mass unit); (2) spike contribution; (3) procedural blank, $15\text{--}30 \times 10^{-12} \text{ g Pb}$ and $0.1 \times 10^{-12} \text{ g U}$. The analysis of the leached minerals was carried out following ref. 14. It includes, after spiking with a ^{205}Pb - ^{233}U tracer, sample dissolution with an HF-HClO_4 mixture, isolation of U and Pb by ion exchange resin, thermoionization of Pb and U with silicagel. Because of the only small amounts available, Pb isotope compositions and U-Pb isotopic dilution data were measured on a secondary electron multiplier. Lines a indicate values corrected for experimental effects: mass discrimination, $0.1 \pm 0.03\%$ per atomic mass unit, spike contribution, analytical contamination. The measured blanks were $25 \times 10^{-12} \text{ g Pb}$, $0.66 \times 10^{-12} \text{ g U}$ when analysing GL1 and CPX and $75 \times 10^{-12} \text{ g Pb}$ and $0.45 \times 10^{-12} \text{ g U}$ when analysing GL2. The measured isotopic composition of the blank was: $^{206}\text{Pb}/^{204}\text{Pb} = 17.85 \pm 0.13$, $^{207}\text{Pb}/^{204}\text{Pb} = 15.58 \pm 0.12$, $^{208}\text{Pb}/^{204}\text{Pb} = 37.67 \pm 0.28$. The blank contribution is expressed in per cent of the ratio (blank/sample corrected for blank) relative to ^{204}Pb and ^{238}U . Lines b indicate the data uncorrected for analytical blank, lines c indicate the recalculated values corresponding to the unleached samples. For all data, the 2σ error concerns the last significant digits. The last two columns indicate the correlation factor (ρ) between isotope ratios, $^{206}\text{Pb}/^{204}\text{Pb} = \alpha$, $^{207}\text{Pb}/^{204}\text{Pb} = \beta$, $^{208}\text{Pb}/^{204}\text{Pb} = \gamma$.

with dilute HBr until the amount of common Pb extracted during this procedure dropped to the analytical blank level, $15\text{--}30 \times 10^{-12} \text{ g Pb}$ (for details see Table 1). The leaching procedure for the second glass aliquot GL2 was carried out after the analyses of the clinopyroxene and glass fraction GL1 and involved many more leaching steps (145 steps instead of 46).

The Pb isotope compositions and the amounts of Pb and U measured in the leachates are summarized in Table 1. For all three mineral fractions the first leaching step extracts several nanograms of Pb with an isotope composition plotting in the field of common terrestrial Pb, which includes most of the major ore deposits and industrial pollutants^{9,10}. The succeeding leaching steps extract decreasing amounts of Pb with a slightly less radiogenic composition but which still lies in the field of terrestrial contaminants. The total amounts of Pb extracted are 13.5 ng for CPX, 8 ng for GL1 and 7.6 ng for GL2, which correspond to Pb contents of 1.8, 0.7 and 1.1 p.p.m. (parts per 10^6), respectively. The leaching procedure also extracts U in small and decreasing quantities, with totals of 0.017 ng for CPX, 0.079 ng for GL1, 0.061 ng for GL2, corresponding to U contents of 2.2, 7.2 and 9.2 p.p.b. (parts per 10^9), respectively.

The measured Pb isotope compositions and Pb-U contents of the leached mineral phases finally dissolved are listed in Table 1 and the linear regressions of the U-Pb data are summarized in Table 2. The leached CPX contains 20 p.p.b. of Pb with a terrestrial Pb isotope composition slightly more radiogenic than that of its first leachate ($^{207}\text{Pb}/^{204}\text{Pb} = 18.5$, $^{207}\text{Pb}/^{204}\text{Pb} = 15.9$, $^{208}\text{Pb}/^{204}\text{Pb} = 37.9$). In contrast the Pb isotope compositions determined in the two glass fractions are highly radiogenic:

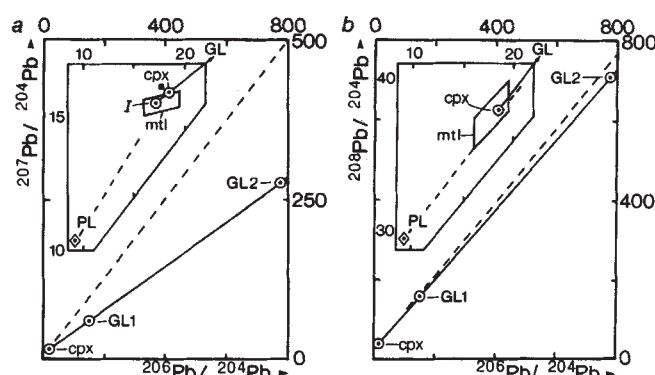


Fig. 1 Pb isotope compositions of the leached minerals. In a, the leached minerals plot on a line corresponding to an age of $3,676 \pm 3$ Myr. In b, the observed alignment defines a $^{232}\text{Th}/^{238}\text{U}$ of 3.4, taking the Pb-Pb age into account. The uncertainty of the data is smaller than the size of the symbols. The dashed line represents the 4,550-Myr closed system evolution for material which has included primordial Pb (PL) and a $^{232}\text{Th}/^{238}\text{U}$ ratio of 3.6. Insets magnify the nonradiogenic parts of the two diagrams. Pb extracted during the leaching procedure and the I component defined from the U-Pb data (Table 2) plot in the field of terrestrial Pb which includes most of the major ore deposits and industrial pollutants^{9,10}. ■, The nonradiogenic Pb component that would be observed had the U-Pb reequilibration during 2 Myr in the silicate inclusion been effective 3,676 Myr ago; it differs from the measured compositions of the CPX leachates and CPX dissolution.

Table 2 U-Pb systematics of the leached minerals

Plot	$Y = a + bX$	Age (Myr)
$X = {}^{206}\text{Pb}/{}^{204}\text{Pb}$	$a = 9.54 \pm 9$	$\rho(a, b) = -0.77$
$Y = {}^{207}\text{Pb}/{}^{204}\text{Pb}$	$b = 0.3430 \pm 6$	$\chi^2_{\text{red}} = 0.81$
	$*a = 9.56 \pm 1$	$\rho(a, b) = -0.86$
	$*b = 0.3427 \pm 7$	$\chi^2_{\text{red}} = 1.11$
$X = {}^{238}\text{U}/{}^{204}\text{Pb}$	$a = 17.21 \pm 12$	$\rho(a, b) = -0.16$
$Y = {}^{206}\text{Pb}/{}^{204}\text{Pb}$	$b = 0.7699 \pm 62$	$\chi^2_{\text{red}} = 0.93$
	$*a = 17.10 \pm 20$	$\rho(a, b) = -0.21$
	$*b = 0.7709 \pm 61$	$\chi^2_{\text{red}} = 0.71$
$X = {}^{235}\text{U}/{}^{204}\text{Pb}$	$a = 15.49 \pm 19$	$\rho(a, b) = -0.33$
$Y = {}^{207}\text{Pb}/{}^{204}\text{Pb}$	$b = 36.39 \pm 33$	$\chi^2_{\text{red}} = 0.71$
	$*a = 15.42 \pm 15$	$\rho(a, b) = -0.36$
	$*b = 36.43 \pm 32$	$\chi^2_{\text{red}} = 0.64$
$X = {}^{206}\text{Pb}/{}^{204}\text{Pb}$	$a = 22.52 \pm 20$	$\rho(a, b) = -0.61$
$Y = {}^{208}\text{Pb}/{}^{204}\text{Pb}$	$b = 0.8904 \pm 14$	$\chi^2_{\text{red}} = 15$
	$*a = 22.11 \pm 19$	$\rho(a, b) = -0.80$
	$*b = 0.8914 \pm 14$	$\chi^2_{\text{red}} = 18$

The 2σ error applies to the last significant digit. The χ^2_{red} values (1σ error) are near 1 except in the plot of ${}^{208}\text{Pb}/{}^{204}\text{Pb}$ versus ${}^{206}\text{Pb}/{}^{204}\text{Pb}$. The latter scatter most likely reflects slightly different Th/U ratios for CPX, GL1 and GL2. The regressions define the non-radiogenic Pb component I : ${}^{206}\text{Pb}/{}^{204}\text{Pb} = 17.2 \pm 0.3$, ${}^{207}\text{Pb}/{}^{204}\text{Pb} = 15.5 \pm 0.2$. In the second part of the centre column, ρ is the correlation factor between a and b .

* Regressions calculated with data that are not corrected for analytical blank.

${}^{206}\text{Pb}/{}^{204}\text{Pb} = 140$ for GL1 and 237 for GL2. Because of the small amount of ${}^{204}\text{Pb}$ present in the sample the values corrected for analytical contamination are significantly higher: ${}^{206}\text{Pb}/{}^{204}\text{Pb} = 150$ for GL1 and 778 for GL2. In the plot of ${}^{206}\text{Pb}/{}^{204}\text{Pb}$ versus ${}^{207}\text{Pb}/{}^{204}\text{Pb}$ (Fig. 1), these three analyses lie on a line corresponding to a Pb-Pb age of $3,676 \pm 3$ Myr. Because of the radiogenic composition measured in the glass, this value is insensitive to the uncertainty of the analytical blank correction (Table 2).

The U concentration in the leached CPX is low, 0.5 p.p.b., whereas the glass shows a much higher concentration of 90 p.p.b. Thus, the ${}^{238}\text{U}/{}^{204}\text{Pb}$ ratio of the CPX is low (1.7) compared with that of the glass (172 for GL1 and 993 for GL2). In the plots of ${}^{206}\text{Pb}/{}^{204}\text{Pb}$ versus ${}^{238}\text{U}/{}^{204}\text{Pb}$ (Fig. 2) and ${}^{207}\text{Pb}/{}^{204}\text{Pb}$ versus ${}^{235}\text{U}/{}^{204}\text{Pb}$, these data lie on lines corresponding to ages of $3,680 \pm 23$ Myr and $3,679 \pm 5$ Myr, respectively. The Pb isotope composition defined by the γ -intercept (I) of these lines (Table 2) is ${}^{206}\text{Pb}/{}^{204}\text{Pb} = 17.2 \pm 0.3$, ${}^{207}\text{Pb}/{}^{204}\text{Pb} = 15.5 \pm 0.2$; it plots in the field of industrial contaminants (Fig. 1).

The isotope composition of Pb extracted during the leaching procedure from the clinopyroxene and glass reveals a major contamination of this inclusion by terrestrial Pb. If the glass had not been leached at all, it would exhibit much less radiogenic Pb: ${}^{206}\text{Pb}/{}^{204}\text{Pb} \approx 25.6$ instead of 150 for GL1 and ≈ 22.0 instead of 236 for GL2 (Table 1). We attribute this contamination to cutting of the iron slice in the presence of liquid—an effect we have discussed previously¹¹. Moreover, the terrestrial isotope composition defined by the Y intercepts of the U-Pb alignments shows that the nonradiogenic component associated with the ${}^{204}\text{Pb}$ measured in the leached samples is a residue of this contamination. Thus two points are clear. First, the observed Pb-Pb and U-Pb alignments are not isochrons *sensu stricto*, but mixing lines between an *in situ* formed radiogenic Pb component and an inherited nonradiogenic terrestrial Pb component. Nevertheless, the slopes of these lines have chronological significance and the concordant ages indicate the closure of the U-Pb system at 3,680 Myr and validate the precise Pb-Pb age. Second, the silicate inclusion does not contain any 'initial Pb'.

The leaching procedure successfully eliminates most of the contaminating Pb. The 46 leaching steps extract 96% of the Pb introduced in GL1 and 99.2% of that in cpx. The more extensive leaching of GL2 leads to a 99.7% decontamination. This decontamination does not disturb the U-Pb system of the glass phase as indicated by the concordant U-Pb ages. However, the leaching procedure dissolves the U and the Th rich withlockite phase which is easily soluble in acid medium⁷. This is indicated by the extraction of U during the first leaching steps.

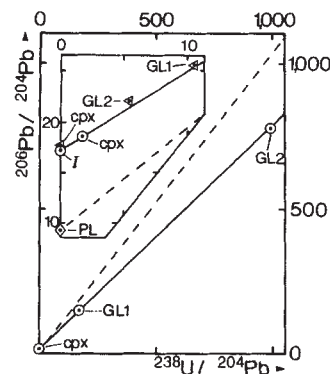


Fig. 2 U-Pb evolution diagram. The leached minerals (circles) lie on a line which defines an age of $3,680 \pm 23$ Myr and the nonradiogenic Pb component I : ${}^{206}\text{Pb}/{}^{204}\text{Pb} = 17.2 \pm 0.3$. The uncertainty of the data is smaller than the size of the symbols. For comparison the dashed line indicates the 4,550 Myr isochron issued from primordial Pb (PL). Inset magnifies the nonradiogenic part of the diagram. Recalculated unleached minerals (triangles), Table 1, plot near, however, on the left side of the line defined by the leached minerals, which may indicate a multiple Pb contamination of this inclusion.

The U-Pb age defined by the leached phases agrees essentially with: the Rb-Sr age of $3,730 \pm 100$ Myr (ref. 1) when recalculated with ${}^{87}\text{Rb} = 1.42 \times 10^{-11} \text{ yr}^{-1}$ and the K-Ar age of $3,500 \pm 100$ Myr (ref. 4); but the U-Pb system defines the age with a factor of 50 better precision.

A complete U-Th-Pb fractionation is associated with the 3,676-Myr event. This is shown by the lack of initial Pb in the inclusion and particularly by the loss of the radiogenic Pb produced between 4,550 and 3,676 Myr. This fractionation was followed by a fast cooling of the silicate inclusion which can be estimated as follows. The radiogenic Pb, which is produced in the inclusion when internal U-Pb reequilibration is effective, must now appear as initial Pb in the CPX; at 3,676 Myr, the production rate of this Pb ($\lambda^{238}\text{U} \cdot [\text{U}] \cdot \text{d}T$) is $1.04 \times 10^{-13} \text{ mol Myr}^{-1} \text{ g}^{-1}$ of glass for the ${}^{206}\text{Pb}$ and $1.03 \times 10^{-13} \text{ mol Myr}^{-1} \text{ g}^{-1}$ of glass for the radiogenic ${}^{207}\text{Pb}$. Taking the ratio of glass to CPX in the inclusion into account (≈ 4), Pb produced during internal reequilibration in 2 Myr would appear in the leached CPX in addition to residual contaminant Pb and the resultant non-radiogenic Pb component should be: ${}^{206}\text{Pb}/{}^{204}\text{Pb} = 17.8$, ${}^{207}\text{Pb}/{}^{204}\text{Pb} = 16.1$. This composition lies outside the field of terrestrial-contaminating Pb and outside the trend which is defined by the leached Pb (Fig. 1). Considering a minimum temperature interval of 200° (800 – 600°C) for the internal reequilibration of Pb, this calculation defines a cooling rate of at least $100^\circ \text{ Myr}^{-1}$. This lower limit agrees with that defined for the metal phase^{6,12}. On the whole, the Pb loss and the instantaneous cooling at 3,676 Myr supports a high-temperature injection of the silicates into the metal phase and the isolation and quenching of this mixture in a small object.

It is difficult to ascertain the origin of the relatively high U and Th contents of the total inclusion, of about 80 p.p.b. U and 300 p.p.b. Th. The U and Th enrichment relative to that of chondritic material (≈ 7) is comparable with that for Sr, 3–5 (ref. 1). This enrichment may have occurred during the early history of the source material or may be the result of the 3,676 Myr event.

The fast cooling of Kodaikanal implies that the Rb-Sr and U-Pb systems were simultaneously closed, 3,676 Myr ago, and confirms that the initial ${}^{87}\text{Sr}/{}^{86}\text{Sr}$ ratio of the inclusions characterizes the Rb/Sr ratio of their source. A more precise redetermination of the Rb/Sr systematics could allow identification of the meteoritic parent body material and evaluation of the agreement between the decay constant values of ${}^{87}\text{Rb}$ and ${}^{235,238}\text{U}$ (ref. 13).

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Microaggregates of non-noble metals and bimetallic alloys prepared by radiation-induced reduction

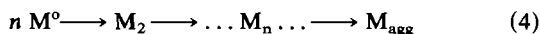
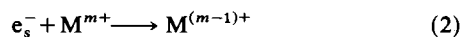
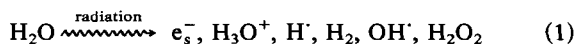
J. L. Marignier*, J. Belloni*, M. O. Delcourt* & J. P. Chevalier†

* Laboratoire de Physico-Chimie des Rayonnements, Associé au CNRS, Université de Paris-Sud, 91405 Orsay, France

† Centre d'Etudes de Chimie Métallurgique, CNRS, 15 rue G. Urbain, 94400 Vitry, France

The high specific area of metallic microaggregates, together with their ability to transfer electrons more readily than the corresponding bulk metals¹⁻⁴, makes this highly dispersed state of matter important in fields such as catalysis, photography and nucleation studies. But the successful preparation of very small microaggregates by radiation-induced reduction of metallic ions has only been reported for noble metals¹⁻⁸. We describe here the extension of the method both to non-noble metals such as Co, Ni, Zn or Pb, where the strong reactivity of the separate metal atoms and native clusters must be overcome, and to bimetallic particles (such as Cu₃Pd) which exhibit perfectly ordered structures⁹. Both kinds of aggregates have many potential applications, the foremost being in catalysis.

Apart from the noble metals, metals with negative redox potentials like Ti (refs 10-12) or Cd (ref. 13) have also been prepared radiolytically as sols which are highly reactive in air and thus could not be investigated by electron microscopy¹¹. Using conditions which ensure optimized yields of noble metals⁶⁻⁸, Ti (ref. 11) or Cd (ref. 13), we have failed to produce microaggregates of other metals, even among the less readily oxidizable ones, such as Ni or Co. Instead, large amounts of molecular hydrogen were produced. The efficiency of the reduction reaction of metal ions M with valency $m+$ by solvated electron (e_s^-) cannot be questioned, since most of the rate constants are quite high^{14,15} (reactions (1) to (3)).



In reaction (4), n is a number of aggregation of a few units and M_{agg} is the aggregate in the final stable state. But reverse oxidation reactions which inhibit the overall reduction process may occur at any stage. Oxidation of transient lower valency states of the metal, by either H_3O^+ (the counter ion of e_s^-), or radiolytic radicals such as $\text{OH}^\cdot$ or even $\text{H}^\cdot$ atoms has been demonstrated^{16,17} in several cases. Finally, the zero valency state, which results from multi-electron transfer (or from dismutation of intermediate valency states) can also undergo oxidation. Even noble metals, such as Ag or Cu, in the form of isolated atoms M^0 or of M_n during the initial stages of aggregate nucleation and

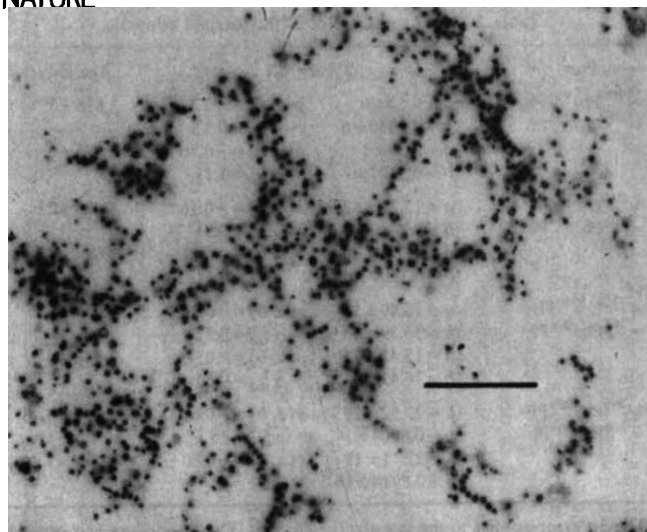
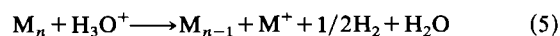


Fig. 1 Low-magnification TEM bright-field image of Ni microaggregates obtained by γ irradiation (dose rate 0.88 Gy s^{-1}) of $\text{NiSO}_4 \cdot 2 \times 10^{-3} \text{ mol l}^{-1}$ in de-aerated water containing $(\text{CH}_2)_2\text{CHOH}$ 0.2 mol l^{-1} and PVA 0.2 mol l^{-1} . The clumps consist of several small crystals. Scale bar, $5,000 \text{ \AA}$.

growth, react² with the medium to produce molecular hydrogen, with a corresponding loss of metal (reaction (5)).



Thus, the development of zero valency aggregates is the result of a competition between this reverse oxidation (reaction (5)) and further aggregation which progressively stabilizes the native metal with respect to its environment (reaction (4)). It is on the basis of this reasoning that we have studied the role of various factors thought to displace the balance of these competing mechanisms towards nucleation and growth⁹.

Experience shows that a successful preparation of non-noble metal microaggregates needs to combine some of the following procedures (which may be limited by metal and/or hydroxide flocculation). (1) Prevent reoxidation processes; this can be achieved through alkalization of the medium (which lowers not only H_3O^+ but also $\text{H}^\cdot$ concentration insofar as the latter may result from an $e_s^- + \text{H}_3\text{O}^+$ reaction) and addition of an $\text{OH}^\cdot$ scavenger (either formate ions or an alcohol like isopropanol, or polyvinylalcohol (PVA)). When both these conditions are used for noble metals, the radiolytic reduction yield G is markedly improved. (2) Induce the aggregation process (if necessary) by adding before irradiation some noble metal such as Pd or Pt (prepared beforehand or *in situ*), in any proportion from a few per cent upwards. (3) Increase the metal-ion concentration to improve G and favour aggregation. (4) Limit the size of aggregates with the aid of a surfactant (if colloidal solutions are wanted) or a support. PVA combines the properties of a surfactant and of an $\text{OH}^\cdot$ scavenger.

The sols thus obtained are stable for several months and do not flocculate, but they fade immediately when brought into contact with oxygen. In the case of Ni and Co, both are ferromagnetic and can be separated using a magnet (the sol can be restored by ultrasonic agitation after removal of the magnet). Once separated, the dried particles can be kept in air provided no water is present.

From the many successful experiments, we shall describe two in greater detail; these are related first to pure Ni, then to a Cu-Pd alloy. In both cases, the dose rate of the ^{60}Co source was $2 \times 10^{19} \text{ eV cm}^{-3} \text{ h}^{-1}$, that is, 0.88 Gy s^{-1} . All chemicals were pure-grade reagents from Merck (isopropanol, CuSO_4 and NaOH used for pH adjustment), Prolabo (NiSO_4), La Compagnie des Métaux Précieux (PdCl_2) and Aldrich (PVA 86000). Specimens for transmission electron microscopy (TEM) are prepared by diluting the sol to reduce the amount of PVA down to $2 \times 10^{-2} \text{ mol l}^{-1}$ and then drying a droplet onto a carbon-coated grid in an inert atmosphere.

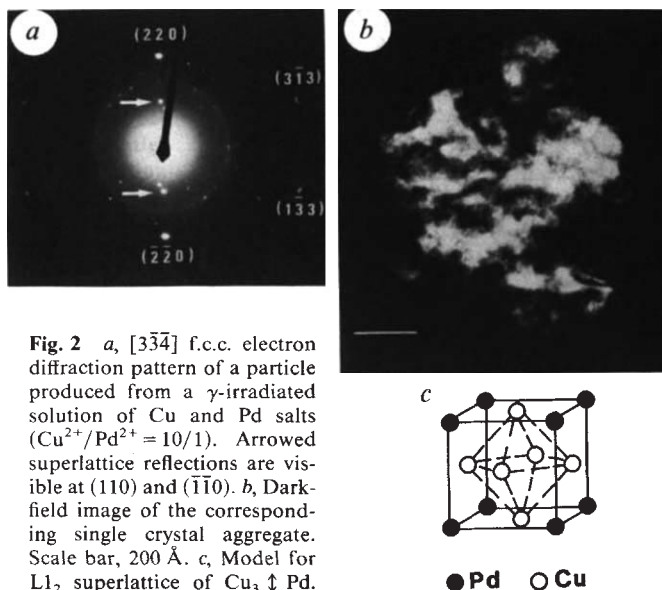


Fig. 2 *a*, $[3\bar{3}4]$ f.c.c. electron diffraction pattern of a particle produced from a γ -irradiated solution of Cu and Pd salts ($\text{Cu}^{2+}/\text{Pd}^{2+} = 10/1$). Arrowed superlattice reflections are visible at (110) and $(\bar{1}\bar{1}0)$. *b*, Dark-field image of the corresponding single crystal aggregate. Scale bar, 200 Å. *c*, Model for L_{12} superlattice of Cu_3Pd .

Pure nickel: A solution of $\text{NiSO}_4 \cdot 2 \times 10^{-3} \text{ mol l}^{-1}$ in de-aerated water containing isopropanol 0.2 mol l^{-1} and PVA 0.2 mol l^{-1} (base monomer) has been irradiated at natural pH = 6.8 up to 205 kGy (20.5 Mrad). Chemical analysis was carried out under nitrogen in a glove-box, by reduction of nitro-blue tetrazolium chloride into monoformazan kept in solution due to PVA and measured by optical absorption. The radiolytic yield, 0.03 Ni atoms per 100 eV, is much lower than for Pt (ref. 6). (Other conditions can be found which lead to much higher values of Ni yield, but so far at most 50% Ni^{2+} has been reduced to metallic Ni (J.B., J.P.C., M.O.D. and J.L.M., in preparation). The subcolloidal solution is brown and highly reactive towards air, but the dried particles can be kept in air without further oxidation as shown by electron diffraction. Figure 1 is a TEM micrograph showing the distribution of polycrystalline clumps of size ranging from ~ 100 to 200 Å . The clumps appear to be embedded in an amorphous substance which may be polymer, but which remains to be identified. Electron diffraction shows Debye rings which can be indexed as Ni f.c.c. structure (face-centred cubic). Small-angle rings are also observed but it has proved impossible to classify these as oxide, hydroxide or sulphate. Higher-magnification dark-field images show that the clumps are made up of several crystal grains of $50\text{--}100 \text{ Å}$ in size, which appear to have twin relation¹⁸.

Cu-Pd alloy: A de-aerated solution containing $\text{CuSO}_4 \cdot 10^{-3} \text{ mol l}^{-1}$, $\text{PdCl}_2 \cdot 10^{-4} \text{ mol l}^{-1}$, isopropanol 0.56 mol l^{-1} and PVA 0.1 mol l^{-1} , pH 10.2 has been irradiated up to 8 kGy. The colloid has a dark green colour (while a pure Cu sol is pink). TEM observations show a very inhomogeneous distribution of particle sizes (ranging from a few hundred Å to $\sim 1 \mu\text{m}$) and structures. Figure 2*a* is an electron diffraction pattern from a large single crystal aggregate, imaged in Fig. 2*b*, which can be indexed as the $[3\bar{3}4]$ orientation of the f.c.c. reciprocal lattice. Moreover, clear superlattice reflections (arrowed) are visible at (110) and $(\bar{1}\bar{1}0)$. This corresponds to the L_{12} superlattice (Fig. 2*c*) of stoichiometric Cu_3Pd . We have also obtained diffraction patterns suggesting a b.c.c. structure (body-centred cubic) and superlattice as well as unknown f.c.c. superlattice; in all cases these clearly imply ordered atomic arrangements. Note that when the initial $\text{Cu}^{2+}/\text{Pd}^{2+}$ ratio is 1 instead of 10 the CuPd superlattice has been observed.

In proper conditions, radiation-induced reduction can produce a wide variety of highly divided metallic materials either pure or alloyed. Extensive applications of these materials are likely to be found, as well as new alloy phases and structures.

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Franciscan Complex Calera limestones: accreted remnants of Farallon Plate oceanic plateaus

John A. Tarduno*, Michael McWilliams*, Michel G. Debiche*, William V. Sliter† & M. C. Blake Jr†

* Department of Geophysics, Stanford University, Stanford, California 94305, USA

† US Geological Survey, Menlo Park, California 94025, USA

The Calera Limestone, part of the Franciscan Complex of northern California, may have formed in a palaeoenvironment similar to Hess and Shatsky Rises of the present north-west Pacific¹. We report here new palaeomagnetic results, palaeontological data and recent plate-motion models that reinforce this assertion. The Calera Limestone may have formed on Farallon Plate plateaus, north of the Pacific–Farallon spreading centre as a counterpart to Hess or Shatsky Rises. In one model², the plateaus were formed by hotspots close to the Farallon–Pacific ridge axis. On accretion to North America, plateau dissection in the late Cretaceous to Eocene (50–70 Myr) could explain the occurrence of large volumes of pillow basalt and exotic blocks of limestone in the Franciscan Complex. Partial subduction of the plateaus could have contributed to Laramide (70–40 Myr) compressional events³.

The Aptian to Coniacian (115–88 Myr) Calera Limestone occurs in coastal California as a belt of blocks in the Permanente Terrane⁴ (Fig. 1). In addition to the limestone, the terrane contains pillow basalt, radiolarian chert of lower Cretaceous (Valanginian) age and continentally-derived greywackes and shale. The limestone is dominantly pelagic, but rare shallow-water oolitic and bioclastic rocks are also found⁵. Pelagic limestone is interbedded locally with pillow lava, tuffaceous breccia, and volcanic sandstone.

The Calera Limestone has two facies, one a light grey limestone interbedded with replacement chert, the other a bituminous black facies. The black facies is lithologically similar to mid-Cretaceous anoxic zones seen on Manihiki Plateau, Hess Rise and Shatsky Rise. This observation led Jenkyns¹ to infer a common depositional environment for the Franciscan and oceanic rocks, and to assign a provisional Cenomanian age to the anoxic part of the Calera Limestone. Together with Pacific plate reconstructions, results from the Deep Sea Drilling Project (DSDP) have led to suggestions that Hess and Shatsky Rises (on the Pacific Plate) had Farallon Plate counterparts, because the crust underlying Hess and Shatsky Rises is the same age as the basement of the respective plateaus⁶.

Henderson *et al.*² suggested that Hess and Shatsky Rises were formed by hotspot activity coincident with the Farallon–Pacific spreading ridge. By analogy with present ridge-coincident hotspots such as the Iceland hotspot which formed paired plateaus,

it is possible that 'mirror images' of Hess and Shatsky Rises formed on the Farallon Plate. The Calera Limestone might then represent obducted slices of carbonate caps deposited on the plateaus.

Well-exposed outcrops of Calera Limestone at Permanente and Pacifica Quarries (Fig. 1) allow models of the origin of the Calera Limestone to be tested. At Permanente Quarry several large limestone sections are repeated by a complex series of faults. At Pacifica Quarry, a continuous 75-m section is exposed in a single block. A black shale horizon is present midway through the section, below which bituminous limestone is interbedded with thin tuffaceous horizons.

The light-grey facies of the Calera Limestone at these quarries dated by planktonic foraminifera as "at least Albian to Turonian"⁷, is now known to extend to the Aptian. Foraminifera from the same sections suggest bathyal depths (200–1,500 m), similar to Hess and Shatsky Rises. Genera present include *Osangularia*, *Gyroidinoides*, *Gavelinella*, *Dorothia* and *Gaudryina*. Sponge spicules, agglutinated foraminifera, and fish debris which would characterize abyssal depths are absent⁸. At both quarries, evidence of shallow water debris is found in the older bituminous limestones. Nearby outcrops of Calera Limestone at Baldy Ryan Canyon near New Almaden also contain oolitic and bioclastic limestone of Albian age, indicating shallow water deposition⁵.

A comparison of stratigraphic columns from Shatsky and Hess Rises, the mid-Pacific Mountains (DSDP Legs 32 and 62 respectively)^{9,10} and the Calera Limestone reveals a similar stratigraphical progression from shallow to mid-bathyal depths. The oldest part of the Calera Limestone, dated by foraminifera from Pacifica and Permanente Quarries, is of Aptian age (115 Myr). By extrapolating sedimentation rates measured above the black shale marker horizon in Pacifica Quarry, we infer that the anoxic sediments below the horizon denote the Barremian–Aptian anoxic zone. As these outcrops probably predate the oldest recovered sediments from Hess Rise (early Albian to late Aptian), it is likely that Pacifica and Permanente Quarry are coeval with Shatsky Rise. The stratigraphy of Site 463 from the mid-Pacific Mountains is most similar to that of the Calera Limestone quarries. A distinctive sequence of Aptian carbonaceous limestone interbedded with tuffs is found at Site 463 and in the Calera Limestone, but is absent in DSDP sites from Hess and Shatsky Rises.

Samples were taken at Permanente Quarry by Courtillot *et al.*¹¹ for palaeomagnetic investigation. In that study, a positive 'mega-conglomerate' suggested that the magnetizations predate block tilting (the palaeomagnetic inclinations are in significantly better agreement after correction to the palaeohorizontal). New palaeomagnetic results from Permanente Quarry which confirm this interpretation are reported below. The age of the sections sampled falls within the Cretaceous normal polarity superchron. Therefore, with facing directions provided by foraminiferal dating, a unique determination of palaeolatitude can be established, assuming that the magnetizations were acquired shortly after deposition.

Thermal and alternating field demagnetization experiments reveal stable magnetizations with blocking temperatures of 500–580 °C, and median destructive fields of 30–40 mT. Magnetizations from 30 palaeontologically-dated samples suggest 7° of poleward translation over the depositional interval of 105–90 Myr (Fig. 2). Palaeolatitudes range from ~18° N at 105 Myr to 25° N at 90 Myr. The palaeolatitude change implies plate speeds of at least of 5 cm yr⁻¹, in accord with estimates of Farallon Plate motion.

Using these new palaeomagnetic data, northern Pacific Basin plate motions^{12–13}, and geological accretion ages, a model terrane trajectory^{14,15} can be computed for the Calera Limestone (Fig. 2). Our preferred model involves the following sequence: (1) Deposition of the Calera Limestone on the Farallon Plate from 105 to 90 Myr between 18° and 25° N. (2) Accretion to North America at 63 Myr. (3) Northward translation relative to North America, driven by

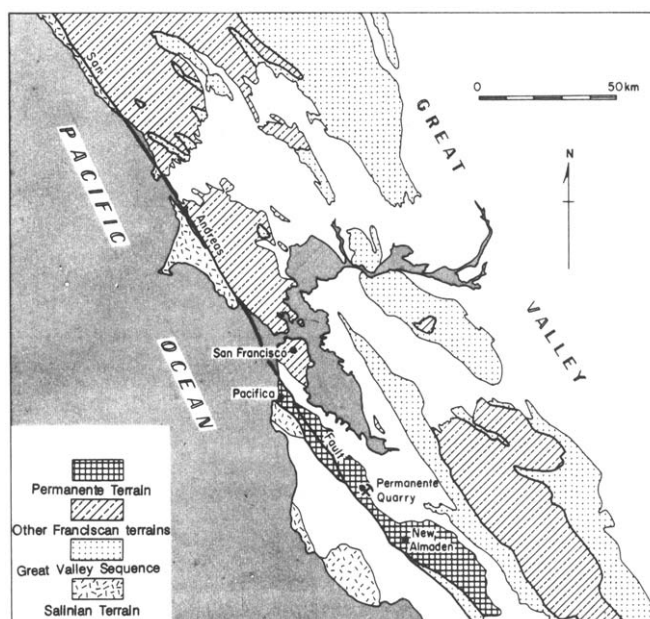


Fig. 1 Location map showing sample localities and regional relations between the Permanente Terrane, other Franciscan terranes, the Great Valley sequence, and the Salinian terrane.

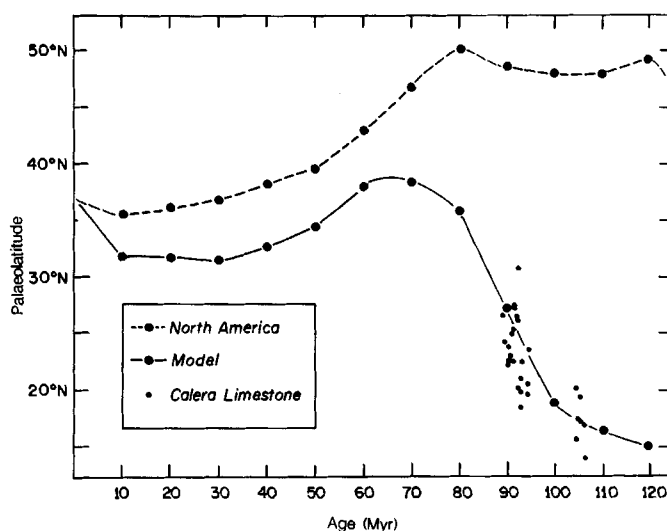


Fig. 2 A terrane model for the Calera Limestone palaeomagnetic data using the plate motion models of Engebretson *et al.*^{12–13} and methods of Debiche *et al.*^{14–15}. The northern option for the initiation of Kula/Farallon spreading has been chosen. Palaeolatitude versus age is shown for 30 palaeontologically dated palaeomagnetic cores (small circles) of Calera Limestone from Permanente Quarry. Scatter in the data probably represents *in situ* slumping. The computed terrane model and the present location of the Calera Limestone on North America are also shown. From 106 to 63 Myr, the Calera Limestone rides on the Farallon Plate converging with North America. At 63 Myr, accretion to North America takes place. From 63 to 10 Myr, the Limestone is driven tangentially along a small circle representing the palaeo-Californian margin with 50% of the coast-parallel Farallon Plate velocity. Pacific Plate motion from 10 Myr to present takes up the final amount of northwards displacement.

oblique subductions of the Farallon Plate from 63 to 10 Myr. (4) Transfer to the Pacific Plate from 10 Myr to the present, after development of the San Andreas transform system.

The palaeopositions of Hess and Shatsky Rises during the known interval of Calera Limestone deposition can be found by reconstructing the Pacific Plate (Fig. 3). If the location of the Farallon-Pacific ridge is accurate, and if spreading is symmetrical, the symmetry between the Calera Limestone and

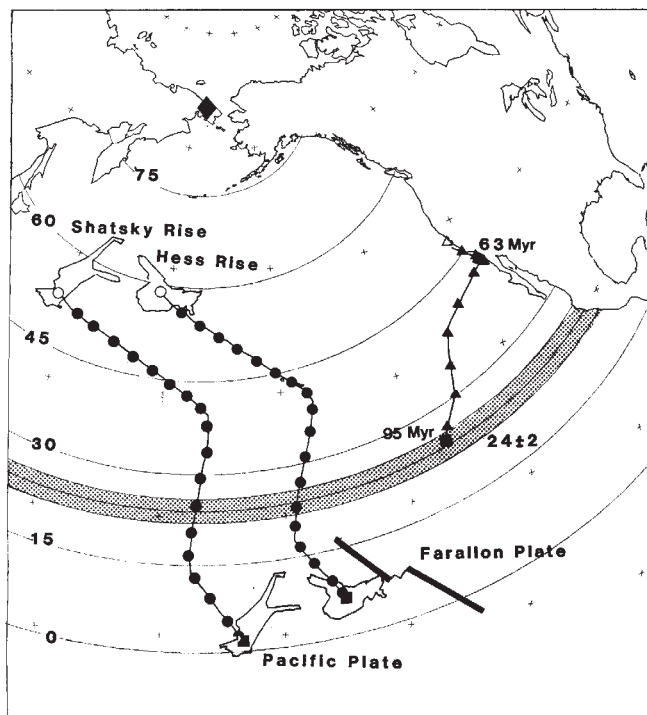


Fig. 3 Oceanic plate reconstruction in fixed North America coordinates is shown for 92 Myr. The small circles represent latitude about a 92 Myr North American pole (solid diamond) interpolated from ref. 18. Tick marks represent the present latitude and longitude coordinates, and the present coastline of Eurasia is shown for reference. Open symbols represent present-day locations while the filled squares represent positions at 92 Myr. Hess and Shatsky Rise are reconstructed back to 92 Myr on the Pacific Plate. The black circles represent 5-Myr increments. The computed terrane trajectory is shown by solid triangles. The stippled region represents the palaeomagnetic constraints for 92 Myr based on a 6-Myr averaging window. This model predicts the crust on which the Calera Limestone was deposited formed during chron M21 (153–154 Myr)¹⁹. Assuming an accurate location of the Farallon-Pacific ridge and symmetrical spreading, this reconstruction suggests that the Calera Limestone originated on a Farallon Plate analogue of Shatsky Rise.

Shatsky Rise astride the Pacific–Farallon ridge suggests that the plateau carrying the Calera Limestone formed as a mirror image of Shatsky Rise.

This overview, together with palaeontological and palaeomagnetic information, suggests a model for the evolution of the Permanente Terrane as a whole. In Kimmeridgian to Albian times (154–105 Myr), topographic highs (a seamount province) were formed on the Farallon Plate, possibly by a hotspot coincident with the Farallon–Pacific ridge. Although the distinction between plateaus, aseismic ridges, and seamounts is partly artificial¹⁶, it is possible that such Farallon Plate topographic expressions attained the dimensions of present oceanic plateaus (800–1,200 km²). General subsidence marked the Albian to Turonian interval (105–90 Myr), with the deposition of pelagic limestones and sporadic off-ridge volcanism.

Accretion in the Franciscan Complex took place in the late Cretaceous to Eocene, marked by the influx of continentally derived greywacke. The partial subduction of buoyant oceanic plateaus and seamounts could have contributed to the shallowing of the angle of subduction which was manifested by Laramide orogenic deformation¹⁷. As the plateaus encountered the trench, the limestone, basalt, and greywacke were obducted and imbricated by thrust faulting. Further northward translation by proto-San Andreas motion, driven by oblique subduction of the Farallon Plate, dissected the obducted limestones and juxtaposed other exotic blocks of limestone, greenstone and chert originally located on more distant parts of the Farallon Plate.

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Contaminated sediments of lakes and oceans act as sources of chlorinated hydrocarbons for release to water and atmosphere

Per Larsson

Institute of Limnology, University of Lund, Box 65, S-221 00 Lund, Sweden

Atmospheric transport is a major route for entry of chlorinated, aromatic hydrocarbons into aquatic ecosystems. Once in the water, the compounds are readily taken up by the biota and distributed in the food webs. Major fractions of the compounds are deposited in the sediment¹, and it had been thought that most persistent contaminants are inactivated in this way as a consequence of their lipophilic properties. However, results from recent laboratory studies^{2,3} raise the possibility that aquatic sediments may not be the final sink for the substances but may rather act as a source through redistribution of the compounds to water and the atmosphere. Polychlorinated biphenyls (PCBs) may be regarded as 'tracers' for these contaminants in the ecosystem, and I studied the transport of PCBs from sediment to water and air in two artificial ponds in the field. The transport from the sediment followed a seasonal cycle; higher concentrations of PCBs in water and air were recorded in the summer and lower in the winter. PCB concentrations in the air over the ponds were positively correlated with PCB levels in the water. My results show that contaminated sediments may act as a source of chlorinated hydrocarbons released into the environment.

In laboratory model systems PCBs are transferred across the sediment/water interface by processes including bioturbation (the activity of benthic macroinvertebrates in the sediment), desorption and gas convection^{2,3}. PCBs also volatilize from water to the air⁴ and a potential cycle of PCBs across the boundaries sediment/water and water/air is thus established. A similar cycle has been proposed for chlorobenzenes in the Niagara River and Lake Ontario⁵.

Transport of PCBs from the sediment to the water and air was studied in large outdoor model ecosystems located in southern Sweden. The systems consisted of two pools (diameter 7.3 m, volume 50 m³), to each of which I added 5–6 tons of lake sediment. The PCB compounds (12 g Clophen A 50, dissolved in 1 l of ethanol) were thoroughly mixed by blending 50 ml of the PCB solution into sections of the sediment. The entire sediment was then stirred with a rake and left for 1 week to

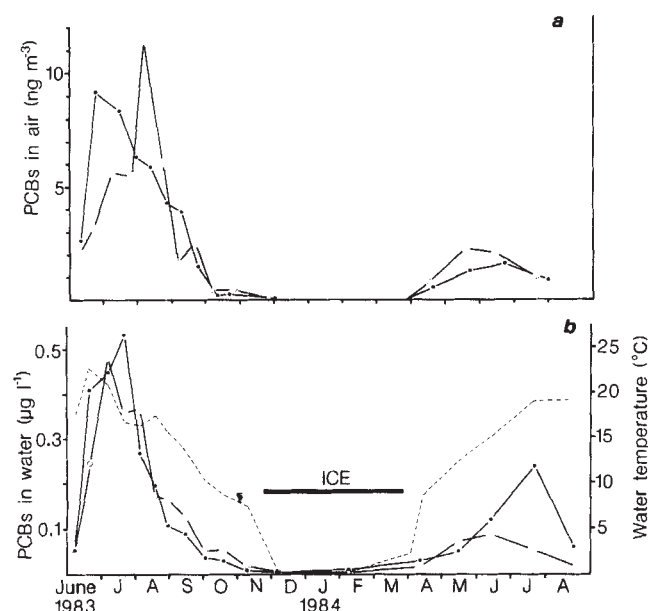


Fig. 1 PCBs in air (a) and in water (b) over the model ecosystems. Filled circles represent the system with fish; unfilled without fish. The dashed line represents water temperature.

stabilize. A theoretical concentration of approximately $2.5 \mu\text{g g}^{-1}$ was thus obtained in the sediment. Water was then added from the nearby river and continuously renewed at a rate of 50 m^3 per month. After 2 months, fish (440 eels, *Anguilla anguilla*, weight 2–5 g and 150 rudd, *Scardinius erythrophthalmus*, weight 1–5 g) were added to one of the experimental ponds.

Levels of PCBs in the water and air were followed by using a filter technique. Twice a month in 1983 and monthly in 1984, about 5 l of water from each pond and from the reference system (containing uncontaminated river water) were passed through polyurethane-foam filters⁶ (PPF) to determine the total PCB fraction, and through particle filters (Whatman GF/C) for quantification of particulate PCBs. PCB transport from water to air was studied by passing air ($\sim 50 \text{ m}^3$ at a rate of 12 l min^{-1}) obtained from directly above the water surface (20 cm) of the pools through particle (Whatman GF/F) and PPF filters connected in series^{7,8}. The procedure was repeated 300 m from the systems to obtain reference air samples (the PCB concentration in these air samples never exceeded 0.6 ng m^{-3}). The PCB compounds adsorbed onto the filters were extracted with hexane⁴ and PCB content determined by capillary-gas chromatography/electron-capture detection^{9,10}.

A fraction of the PCB compounds originally added to the sediment ($2.7\text{--}3.8 \mu\text{g per g dry weight}$) was transported into the water (Fig. 1). The transport followed a seasonal cycle with higher levels in the summer and lower levels in the winter. The processes that transfer PCBs across the sediment/water interface (bioturbation, desorption and gas convection) are positively related to temperature and may all be involved in the transport. In the reference system, concentrations of PCBs in the water were considerably lower, never exceeding $0.002 \mu\text{g l}^{-1}$. Particles in the water adsorbed $39 \pm 21\%$ ($n = 22$) of the PCBs. In general more PCBs were adsorbed to particles in the summer (probably to phytoplankton) than in the winter.

A greater loss of PCBs from sediment to water occurred in the first year than in the second. This difference may be explained by lower bioturbation in 1984 than in 1983 as the benthic fauna was reduced by a factor of 10 (from 5,000 to 500 chironomid larvae per m^2), probably due to predatory invertebrates and fish. The lower levels may also be a result of accumulation of allochthonous material (such as leaves and pollen) on top of the PCB-containing sediment, thereby reducing the rate of transport. On a longer timescale, the PCB concentration in the water should decrease according to a damped oscillation with higher losses

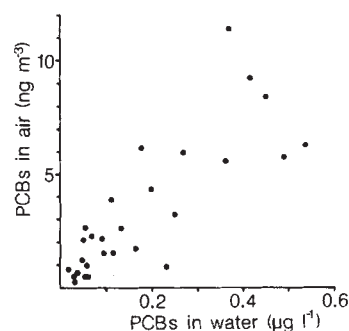


Fig. 2 Correlation of the levels of PCBs in the water and in air over the model ecosystems.

in the summer than in the winter. Of the PCBs originally added to the sediment, 0.5–0.7% had been transferred to the water after 15 months.

The fall in PCB concentrations in the water from summer to winter and from the first to the second year was reflected in the amounts of PCBs taken up by the zooplankton. Uptake of PCBs by *Daphnia magna* followed a positive, linear relation ($r^2 = 0.90$, $F = 261$, $P < 0.001$).

The levels of PCBs in the air over the experimental ponds were elevated compared with the reference area (Fig. 1). The dominating transfer process for PCBs across the water/air interface is probably volatilization, as maximum concentrations were recorded in air at high water temperatures (20°C). This was further supported by the observation that PCBs with four or less chlorine atoms per molecule of the technical PCB mixture achieved a higher concentration in the air than those with five or more chlorine atoms⁴. Furthermore, the majority of the air-borne PCB fraction was presumably in the gas phase ($>90\%$) as it passed the particle filters. A similar relation has been shown in air over Lake Michigan¹¹.

In the winter, the volatilization of the compounds is prevented by ice. After ice break-up the concentration of PCBs in the air rose with both increasing temperatures and increasing PCB levels in the water. Concentrations of PCBs in air were lower the second year than in the first because of lower overall levels in the water during the second year.

The concentrations of PCBs in the air were positively correlated with the levels in the water (Fig. 2, $r_s = 0.84$, $P < 0.001$, Spearman rank correlation). As the extended relation probably follows Henry's law and its extension into fugacity models¹², temperature partly governs the relation. Levels of PCBs in the water of lakes and oceans will therefore be reflected in the atmosphere.

The flow of PCBs from water to air was studied by enclosing an air volume over a defined water surface with a box open towards the surface microlayer. PCB-free air (that had been passed through two PPF filters) was continuously passed over the surface and compounds leaving the water were trapped on a PPF filter. In October 1983 the flow of PCBs was 47 ng per m^2 per day (s.d. = 24, $n = 4$) and in April 1984 in similar conditions the flow was 59 ng per m^2 per day (s.d. = 28, $n = 5$). At the same time the air-borne fallout (as measured using two silicone nets¹³) was $22 \text{ ng PCBs per m}^2$ per day. Consequently, the aquatic model systems acted as a source of PCBs released to the atmosphere.

These results show that lipophilic compounds of low volatility such as PCBs may leave the sediment and contaminate water and atmosphere for a considerable time. Through air-borne fallout and sedimentation¹⁴, the compounds are then again transferred to the sediment, continuing the cycle of chlorinated hydrocarbons in the ecosystem.

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Oxygen isotope ratios in N_2O from nitrification at a wastewater treatment facility

T. Yoshinari & M. Wahlen

Wadsworth Center for Laboratories and Research, New York State Department of Health, Albany, New York 12201, USA

Atmospheric N_2O plays an important part in the destruction of ozone in the stratosphere¹ and influences the troposphere heat budget². Although the emission of N_2O formed by nitrification^{3,4} and denitrification⁵ from soil and aquatic environments has been considered and rates of production and destruction estimated⁶, the strengths of different sources and sinks of NO_2 for a global budget have yet to be successfully assessed. This is mainly because the number of measurements and the areal coverage have been limited. We proposed previously⁷ a comparison of the $^{18}O/^{16}O$ ratio of N_2O from different sources with that of the atmosphere for the evaluation of source strengths. We report here that the $\delta^{18}O$ in N_2O predominantly produced by nitrification in a wastewater treatment facility was significantly lower than that of atmospheric N_2O . This suggests that the $\delta^{18}O$ of atmospheric N_2O cannot be explained by formation and release from nitrification alone. There must be other important sources or mechanisms that cause higher values of $\delta^{18}O$ in atmospheric N_2O .

To determine the oxygen isotope composition in N_2O produced during ammonia oxidation, we analysed the air from enclosed housings of a wastewater treatment facility (Smithtown, Long Island, New York) equipped with rotating biological contactors where nitrification is actively taking place^{8,9}. Nitrifying bacteria in the biofilm on the large surface areas of the contactors efficiently oxidize ammonia to nitrate via nitrite.

The facility consists of two identical treatment trains set up in parallel with a total processing capacity of 1,400 m^3 per day. Two flow-through treatment tanks with rotating biological contactors are connected in series in each train, as schematically illustrated in Fig. 1a. Each tank is enclosed in a dome-shaped fibreglass housing with several small windows on both sides for air intake. Air and water samples were collected at locations indicated in Fig. 1a.

The air in the housings was collected into scuba diving tanks by using a portable compressor on 27 July 1984. Before sequential sampling of the air in both housings, all the windows had been closed to minimize the influx of outside air. The measured N_2O concentrations in the air samples collected at different times are shown in Fig. 2 and Table 1. The procedure for separation of N_2O from the large volume air samples and the measurement of isotope ratios by high resolution infrared laser spectroscopy were described previously⁷. Analyses of ammonia, nitrite, nitrate, total nitrogen, and organic carbon and nitrogen were performed by standard techniques (Table 2 and refs 12-14). N_2O concentrations in air from each scuba tank were determined by gas chromatography with electron-capture detector¹⁰.

Analyses from both treatment plant housings (numbers 1 and

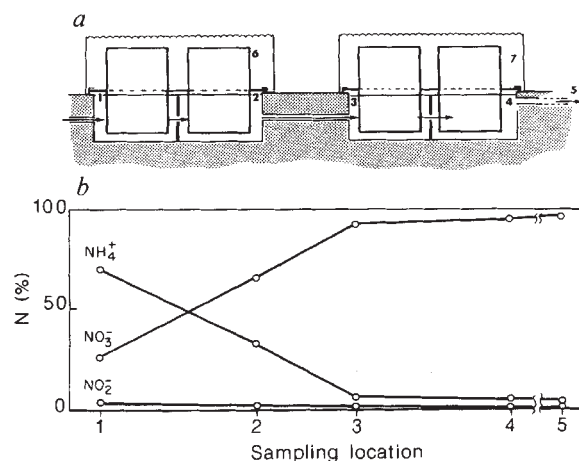


Fig. 1 a, Schematic diagram of treatment facility, showing one of two identical treatment trains set up in parallel. Two flow-through treatment tanks with rotating biological contactors are connected in series and each unit is enclosed in a dome-shaped fibreglass housing. Locations where air and water samples were collected are indicated with numbers 1-7. Net volume of each treatment tank and net air space of each housing were about 42 m^3 and 72 m^3 , respectively. b, Relative abundance of N (%) as NH_4^+ , NO_2^- and NO_3^- in waters collected at sites numbered as in a. These data are based on the results in Table 2.

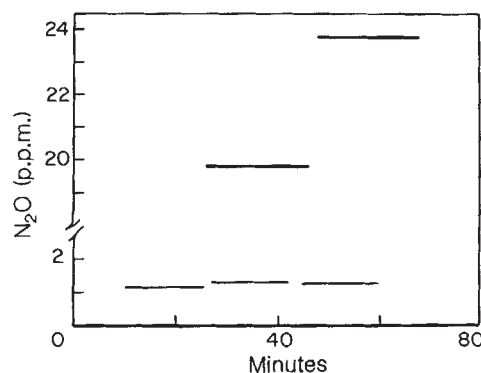


Fig. 2 The time required for filling air sample in each scuba tank and the measured N_2O concentrations in these scuba tanks. Thick and thin lines represent the samples collected at locations 6 and 7, respectively, in Fig. 1a. Windows of each housing were closed at $t = 0$ to minimize the influx of outside air.

2) are compared in Table 1 with earlier results from air samples collected in Albany, New York, and nearby rural areas, as well as for a soil gas sample from a heavily fertilized plot⁷. Both concentrations of N_2O and values of $\delta^{18}O$ in N_2O from housing 1 were substantially different from those of atmospheric N_2O . The N_2O concentrations were ~70 times higher than in ambient air, and the values of $\delta^{18}O$ averaged 22.4‰ (Table 1). Data on nitrogen species and organic nitrogen and carbon in wastewater sampled from the inlets and outlets of the tanks are shown in Table 2. Based on the results in Table 2, the relative abundance of N in forms of ammonia, nitrite and nitrate at the five sites is also illustrated in Fig. 1b.

Examination of the nitrogen budget between the inlets of both tanks shows that ammonia was almost quantitatively oxidized to nitrate via nitrite (Table 2 and Fig. 1b). As there is no indication of appreciable nitrate reduction, it is unlikely that a substantial quantity of N_2O is released from the first tank by denitrification. Therefore, we conclude that the N_2O in housing 1 is mainly a by-product of nitrification.

The fact that $\delta^{18}O$ values for N_2O in the air of housing 1 were distinctly lower than the average value observed in ambient air samples (Table 1) is consistent with the assumption that

Table 1 N₂O concentrations and $\delta^{18}\text{O}$ of N₂O in air samples in two housings of sewage treatment facility, and those of soil gas and ambient air

Samples	N ₂ O concentrations (p.p.m.)	$\delta^{18}\text{O}$ in N ₂ O (% SMOW)
Sewage treatment facility		
Housing 1	19.81 ± 0.14	23.1 ± 1.1
	23.74 ± 0.18	21.7 ± 2.2
Housing 2	1.18 ± 0.02	
	1.31 ± 0.03	36.1 ± 1.3
	1.29 ± 0.02	
Soil gas	0.57 ± 0.01	35.9 ± 0.4
Ambient air, Albany	0.31 ± 0.01	45.4 ± 1.0

N₂O concentration in each tank was determined by gas chromatography with an electron-capture detector¹⁰. The sample was filled manometrically into a calibrated loop (~1 ml) of a six-port valve, and then injected into the main stream of a gas chromatograph by switching the valve position. $\delta^{18}\text{O}(\%) = [({}^{18}\text{O}/{}^{16}\text{O})_{\text{sample}}/({}^{18}\text{O}/{}^{16}\text{O})_{\text{SMOW}} - 1] \times 10^3$ where SMOW is Standard Mean Ocean Water¹¹. Values of $\delta^{18}\text{O}$ were also determined for each scuba tank except samples of three tanks from housing 2 were combined for the measurement. Experimental uncertainties are ±1 s.e.m. from multiple measurements. Data of soil gas and ambient air are taken from ref. 7.

$\delta^{18}\text{O}$ values in N₂O produced from nitrification should have a relatively light oxygen isotope composition, as the two oxygen atoms incorporated into nitrite in the oxidation of ammonia by *Nitrosomonas europaea* are equally derived from O₂ and H₂O (refs. 15, 16), and as N₂O appears to be formed mostly from the reduction of nitrite when the partial pressure of dissolved oxygen is small¹⁷. The average value of $\delta^{18}\text{O}$ of 22.4% in the air samples from housing 1 compares well with a value of ~24% for the 'pure' soil N₂O component in a soil gas/air mixture, estimated from the observed $\delta^{18}\text{O}$ in the N₂O, the excess of N₂O, and $\delta^{18}\text{O} = 45\%$ for atmospheric N₂O (ref. 7). Because this gas was collected from a field heavily fertilized with manure, it was also inferred that the N₂O in the soil gas was produced largely from nitrification⁷.

In the second tank little changes in the concentrations of nitrogen compounds were observed (Table 2). The N₂O concentration in the air of housing 2 (1.2 parts per million, p.p.m.) was only about four times higher than in ambient air, and $\delta^{18}\text{O}$ in N₂O was 36.1% (Table 1). If the N₂O in the second housing were of the same type as in the first housing, an oxygen-18 balance, using the indoor and atmospheric N₂O concentrations and $\delta^{18}\text{O}$ values from Table 1, predicts the $\delta^{18}\text{O}$ in N₂O of the second housing to be 27.9%. The measured $\delta^{18}\text{O}$ of 36.1% is clearly higher, suggesting some contribution of 'heavier' N₂O, derived perhaps from the enrichment by partial reduction of N₂O. Oxygen-18 enrichment in residual N₂O has been observed earlier for the denitrifying bacterium *Pseudomonas aeruginosa* in laboratory conditions⁷.

The yield of N₂O (the ratio of the amount of nitrogen transformed into N₂O to the amount of nitrogen oxidized from ammonia to nitrate) can be estimated as follows. From the data in Fig. 2 the rate of the increase of N₂O concentration in housing 1 was estimated to be 3.2×10^{-3} p.p.m. s⁻¹. With a net air space of 72 m³ this is equivalent to a N₂O production rate of 2.9×10^{-4} g N s⁻¹. Assuming that the rate of ammonia oxidation to nitrite is rate-limiting, the nitrogen transformation rate calculated from net tank volume (42 m³), water flow rate (8.1×10^{-3} m³ s⁻¹) and the average difference of ammonia and nitrate concentrations at the inlets of the two tanks (Table 2) was 1.0×10^{-1} g N s⁻¹. The N₂O yield then becomes 2.9×10^{-3} . This estimate is somewhat lower than the value of 4.7×10^{-3} obtained from laboratory studies using *N. europaea* in soil under the condition of low oxygen tension³. However, it is comparable with an average value of 3.3×10^{-3} from *in situ* measurements in the Potomac

Table 2 Concentration of nitrogen species and total organic carbon in sewage samples at various points of the treatment train

Forms of nitrogen (mg N per litre) and carbon (mg C per litre)					
Sample no.	NH ₄ ⁺	NO ₂ ⁻	NO ₃ ⁻	Organic N	Total organic C
1	13.25 ± 0.25	0.69 ± 0.01	5.00 ± 0.11	14.7 ± 0.4	48 ± 3
2	5.78 ± 0.18	0.36 ± 0.01	11.50 ± 0.13	10.2 ± 0.3	32 ± 2
3	0.84 ± 0.14	0.19 ± 0.01	12.45 ± 0.38	10.2 ± 0.3	35 ± 2
4	0.64 ± 0.15	0.06 ± 0.01	12.75 ± 0.32	10.0 ± 0.3	31 ± 2
5	0.44 ± 0.03	0.10 ± 0.01	12.15 ± 0.20	—	18 ± 1

Sample numbers as in Fig. 1a. Wastewater samples were collected in clean plastic bottles and immediately frozen. Analysis of ammonia, nitrite and nitrate concentrations were performed by Nesslerization, diazotization and brucine methods, respectively¹². The concentrations of organic nitrogen were calculated by subtracting the concentrations of ammonia nitrogen from those of total Kjeldahl nitrogen, which was measured by the indophenol blue method after sample digestion¹³. Total organic carbon was determined by the ultraviolet-oxidation method and CO₂ measurement with an infrared analyser¹⁴. Experimental uncertainties are ±1 s.e.m. from multiple measurements.

River¹⁸ and an estimate of 2.9×10^{-3} derived from studies in the Central Pacific¹⁸. A lower value of 1.2×10^{-3} was reported in the Sargasso Seas where the biological activity is low¹⁹.

The results presented here suggest that N₂O from nitrification has a $\delta^{18}\text{O}$ of ~22%, which is substantially lower than 45% for N₂O in the atmosphere. If N₂O from nitrification is indeed a significant source for atmospheric N₂O, a source of isotopically heavier N₂O, possibly from denitrification is required to balance the atmospheric N₂¹⁸O. N₂O from the oceans, which at the oxygen minimum layer is thought to be largely derived from nitrification¹⁸⁻²⁰, could have a slightly higher $\delta^{18}\text{O}$ because dissolved O₂ (ref. 21) and ocean water are somewhat heavier in $\delta^{18}\text{O}$ than atmospheric O₂ and meteoric water.

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Vent-type taxa in a hydrocarbon seep region on the Louisiana slope

Mahlon C. Kennicutt II, James M. Brooks,
Robert R. Bidigare, Roger R. Fay,
Terry L. Wade & Thomas J. McDonald

Department of Oceanography, Texas A & M University,
College Station, Texas 77843, USA

Recent discoveries on the northern Gulf of Mexico continental slope have altered our understanding of biological and chemical processes occurring in the deep ocean. A biological community of hydrothermal vent-type organisms was recently discovered at the base of the Florida Escarpment¹, where the fauna are apparently nourished by hydrogen sulphide-rich hypersaline water seeping out onto the sea floor. Dense colonies of deep living chemosynthetic benthic organisms were first discovered during investigations of warm water anomalies along the axis of the Galapagos Rift in the Pacific Ocean in 1977²⁻⁴, and this first discovery of clusters of clams, tube worms and other filter feeders in the immediate proximity of warm water vents has been followed by the discovery of a number of other hydrothermal vent sites, for example Guaymas Basin, East Pacific Rise at 21° N. The dense population assemblages at these sites are apparently restricted to small areas of the ocean floor where hydrogen sulphide-rich water is escaping from spreading centres, but the Florida Escarpment discovery indicates that these communities can also exist on passive margins. Here we report the discovery of dense biological communities associated with regions of oil and gas seepage on the Louisiana continental slope. These communities of large epi- and infaunal organisms are similar to those associated with the vents of the Pacific and the hypersaline brine seeps of the Florida Escarpment. Carbon isotope analyses suggest that these communities are chemosynthetic and derive their energy from hydrogen sulphide and/or hydrocarbons. Similar communities may be widely distributed on the sea floor in other oil-producing regions of the ocean.

In July 1984, we reported the discovery of thermogenic gas hydrates in marine sediments from the Louisiana slope⁵. These hydrates were associated with oil-stained cores similar to those found at a nearby location⁶. Based on the widespread occurrence of oil-stained cores (containing up to 15% extractable organic matter) in the Green Canyon lease area (~27°–28° N and 90°–92° W) and the flux of hydrocarbons into the overlying waters, two benthic trawl samples were taken to determine the effect of these hydrocarbons on the benthic communities (see Fig. 1 for locations). Populations of hydrothermal vent type organisms were recovered in both trawls including bivalves, gastropods and vestimentiferan tube worms.

Our first trawl was taken near 27°40' N and 91°32' W at water depths between 600 and 700 m just south of an area known to contain oil-stained sediments and thermogenic gas hydrates⁵. The site was chosen because of a large seismic 'wipeout' zone where the stratifications of the sediments are masked (Fig. 2) and the presence of a persistent oil slick at the surface (presumably caused by sea bottom oil seepage). Coring of these seismic wipeout zones in the Green Canyon area have consistently recovered oil-stained, gas charged and/or gas hydrate-containing sediments. The 10-m semi-balloon otter trawl was on the sea bottom for ~60-min over a 3.5-nautical mile-long track. This track crossed a ~2.0-n. mile-wide wipeout zone. The first trawl contained 800 kg of bivalve and gastropod shells, including both living and disarticulated bivalves ranging from 5 to 10 cm in length. The haul contained 30% living bivalves, 60% disarticulated bivalves and 10% living gastropods. Organisms collected in our first trawl included the bivalves *Calyptogena ponderosa*, *Vesicomya cordata*, *Lucinoma atlantis* and an unidentified neogastropod. Both *Calyptogena* and *Vesicomya* contain haemoglobin.

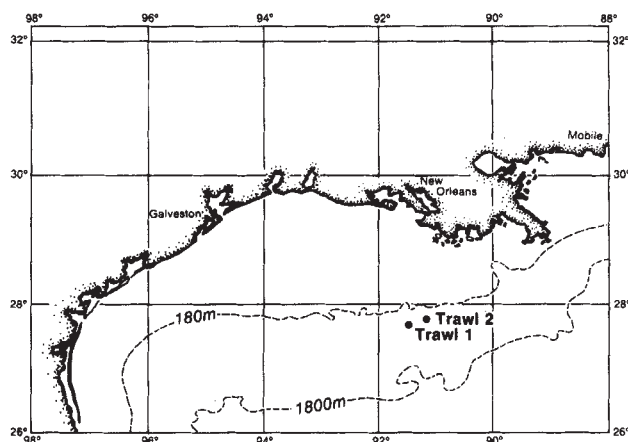


Fig. 1 Trawl locations on the Gulf of Mexico slope.

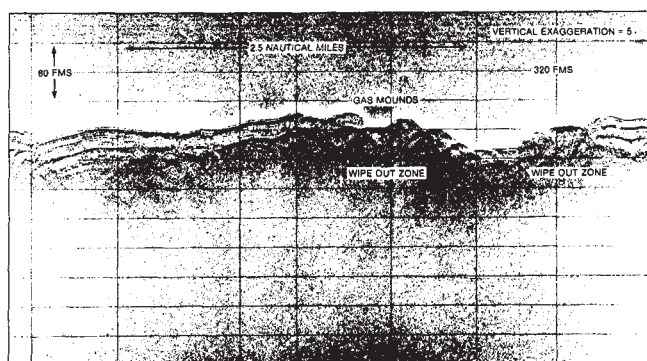


Fig. 2 Acoustical record (3.5 kHz) along the track of trawl one. Wipe-out zones represent areas of oil, hydrate and/or gas-charged sediments. The wipeout zones are thought to be the locations of the chemosynthetic ecosystems.

The second trawl (~27°45' N and 91°14' W) was taken in the region where Anderson *et al.*⁶ previously reported oil-stained cores. Seismic data and additional cores obtained in this region confirmed the occurrence of hydrocarbon seepage. The trawl covered a distance of ~2.5 n. miles and crossed a second seismic wipeout zone. The trawl contained an entanglement of vestimentiferan tube worms (*Lamellibrachia* sp.) with various gastropods and bivalves. The vestimentiferans recovered in the trawl were ~2.0 m long and up to 1 cm in diameter. The organisms in this second trawl included *Acesta bullisi*, *L. atlantis*, *Gaza fischeri* and the same unidentified neogastropod as retrieved in the first trawl. Both trawls also contained significant numbers of crabs, shrimp and fish that have yet to be identified. The tube worms and gastropods recovered from these trawl sites are taxonomically different from those reported for the Florida Escarpment and the Galapagos Rift. However, one of the vesicomyid clams (*C. ponderosa*) collected at the first trawl site belongs to the same genus as the clams found at the Florida Escarpment (*Calyptogena* sp.), Galapagos Rift (*Calyptogena magnifica*) and Guaymas Basin (*Calyptogena pacifica*).

Carbon isotope analyses were performed on selected organisms to determine their food source (Table 1). Stable carbon isotopes are useful in delineating the flow of carbon through ecosystems as there is considerable evidence for minimal carbon isotope fractionation along marine food chains⁷⁻¹⁰. Organisms that feed on photosynthetically derived carbon from marine algae have carbon isotope values ranging from -19 to -21‰ (Table 1 and ref. 11). Tissue from mussels recovered at the

Table 1 Carbon isotope values ($\delta^{13}\text{C}$ in ‰ relative to PDB) for organisms obtained from trawls on the Gulf of Mexico continental slope.

Organisms	Description	Station	Depth (m)	$\delta^{13}\text{C}$ (‰)	Position		Comment
<i>Geryon quinquedens</i>	Crab	E-1	390	-17.2	28°24' N	85°58' W	
<i>Bembrops gobioides</i>	Fish	E-1	390	-17.8	28°24' N	85°58' W	
<i>Synaphobranchus brevidorsalis</i>	Eel	E-3	840	-18.1	28°11' N	86°26' W	
<i>S. brevidorsalis</i>	Eel	E-4	1,225	-19.2	28°07' N	86°36' W	
<i>Bathypterois guardrifulis</i>	Fish	E-4	1,225	-18.6	28°07' N	86°36' W	
<i>Synaphobranchus oregoni</i>	Eel	E-4	1,225	-19.5	28°07' N	86°36' W	
<i>Nematocarcinus rotundus</i>	Shrimp	E-4	1,225	-18.2	28°07' N	86°36' W	
<i>Acanthephyra eximia</i>	Shrimp	E-4	1,225	-18.3	28°07' N	86°36' W	
<i>G. quinquedens</i>	Crab	E-4	1,225	-19.3	28°07' N	86°36' W	
<i>S. oregoni</i>	Eel	C-1	345	-19.6	28°03' N	90°15' W	
<i>G. quinquedens</i>	Crab	C-4	1,390	-17.4	27°28' N	89°44' W	
<i>Bathygadus macrops</i>	Fish	W-2	550	-17.5	27°25' N	93°19' W	
<i>Monomitopus</i> sp.	Fish	W-3	790	-18.1	27°08' N	93°24' W	
<i>Dicrolene</i> sp.	Fish	W-3	790	-18.3	27°08' N	93°24' W	
<i>Halosaurus guentheri</i>	Fish	W-3	790	-17.5	27°08' N	93°24' W	
<i>Stereomastis sculpta</i>	Shrimp	W-4	1,390	-17.0	26°44' N	93°19' W	
<i>Calypotgena ponderosa</i> *	Clam	42	600	-35.4 -35.3	27°40' N	91°32' W	Seep area
<i>Lucinoma atlantis</i> *	Clam	42	600	-31.2 -33.0	27°40' N	91°32' W	Seep area
Unidentified neogastropod	Snail	42	600	-31.5	27°40' N	91°32' W	Seep area
<i>Lamellibrachia</i> sp.	Tube worm flesh	43	600	-27.0	27°45' N	91°14' W	Seep area
<i>Lamellibrachia</i> sp.	Worm tube	43	600	-28.1	27°45' N	91°14' W	Seep area
<i>Nezumia aequalis</i>	Fish†	42	600	-17.6	27°40' N	91°32' W	Seep area
<i>Monomitopus</i> sp.	Fish	42	600	-17.9	27°40' N	91°32' W	Seep area
<i>Chaunax pictus</i>	Fish	42	600	-17.9	27°40' N	91°32' W	Seep area
<i>Coryphaenoides colon</i>	Fish	43	600	-17.2	27°45' N	91°14' W	Seep area

Carbon isotopes samples were prepared in a Craig-type combustion system with CO_2 determination on a Finnigan MAT 251 isotope ratio mass spectrometer. Depths are approximate as many areas of the slope are steep.

* $\delta^{13}\text{C}$ values were determined on two individuals.

† Fish were not necessarily collected in the immediate vicinity of the seeps but could have been collected at other areas during the trawl.

Pacific vents have $\delta^{13}\text{C}$ values near -33‰ (refs 12-14). The vent communities of the Pacific are based on chemoautotrophic bacteria that gain energy from the oxidation of hydrogen sulphide¹⁵⁻¹⁸. In turn, the associated filter-feeding organisms feed on these isotopically light bacteria. Internal symbiotic bacteria are found in clams, mussels and vestimentiferans from the hydrothermal vents¹⁹ and are probably present in the gills of the bivalves as well as the vestimentiferan worms at this site.

Carbon isotope analysis of freeze-dried mantle and foot tissue of bivalves from the first trawl had $\delta^{13}\text{C}$ values of -31 to -35‰. This suggests that the food source of these animals results, at least in part, from chemosynthesis rather than terrestrial or marine photosynthetic organic carbon. These isotope values provide supporting evidence that the food source of the bivalves is sulphur- or hydrocarbon-oxidizing bacteria in this hydrocarbon/sulphide-rich environment ($\delta^{13}\text{C}$ of the oil and methane is -26.5 and -45‰, respectively). The bivalves smelled strongly of hydrogen sulphide during dissection. The vestimentiferan worms and their tubes collected in the second trawl have $\delta^{13}\text{C}$ values of -27 and -28‰, respectively. In comparison, tube worms (*Riftia pachyptila*) sampled from the Galapagos Rift had considerably heavier isotope values (-11‰; ref. 12). One explanation for these heavier isotope values is that internal symbiotic chemosynthesis in tube worms limits the supply of CO_2 , thus reducing isotope fractionation. The oil-seep tube worms must also have a mechanism of carbon assimilation that reduces isotope fractionation relative to the bivalves.

This report significantly expands the geographical area in which one would expect to find dense hydrothermal vent-type taxa in the deep ocean. It also suggests that oil and gas seeping to the surface from deeper hydrocarbon reservoirs can support, by chemosynthesis, vent-type organisms in the deep ocean. Hydrocarbon seepage occurs in many shelf and slope regions, thus making it probable that these communities are more widely distributed than previous discoveries have suggested. As these sites are studied further, several new species may be found (R. Turner and M. Jones, personal communication).

This discovery is distinct from those in Pacific hydrothermal

vents and Florida Escarpment communities in several ways. First, the source of reduced compounds (possibly hydrogen sulphide, hydrocarbons and/or ammonium) is not a point source. The seepage is diffuse and occurs over a wide area in the seismic wipeout zones. It is impossible to determine from trawl catches whether the organisms are living in the seep area or along its perimeter. Second, the biological assemblages are associated with seeping hydrocarbons that have significant toxicities (particularly aromatic hydrocarbons). Third, these chemosynthetic communities are not at abyssal depths. Fourth, water temperatures are not elevated. The high productivity at the hydrothermal vent communities seems to be sustained by high bacterial turnover rates in the high-temperature vent plumes¹⁸. It is not known how hydrocarbons effect bacterial production rates. Finally, the shallower seep taxa reported here may serve as a food source for various deep-sea organisms. Further study is needed to elucidate: (1) how and to what extent the taxa adapt themselves to high hydrocarbon environments; (2) how widespread geographically these organisms are on the Louisiana slope, as well as other oil-producing regions; and (3) how significant a biomass contribution they make to the deep sea.

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Regulated progression of a cultured pre-B-cell line to the B-cell stage

Michael G. Reth*, Patrizia Ammirati, Sharon Jackson & Frederick W. Alt

Department of Biochemistry and Institute for Cancer Research, College of Physicians and Surgeons of Columbia University, New York, New York 10032, USA

The variable (V) regions of heavy and light immunoglobulin chains are encoded by multiple germline DNA elements which are assembled into complete variable-region genes in precursor(pre-) B lymphocytes¹. The heavy-chain V region (V_H) is assembled from three separate germline DNA elements, the variable (V_H), diversity (D) and joining (J_H) segments; whereas light-chain variable regions of either the κ or λ type are assembled from two elements, the V_L and J_L . Analysis of tumour cell lines or sorted cell populations which represent early and late pre-B cells has suggested that heavy-chain assembly and expression generally precedes that of light chains²⁻⁵; but, primarily because of the lack of appropriate model systems to study the phenomenon, the mechanism and significance of this apparently orderly differentiation process are much debated. Here we describe for the first time a transformed cell line, 300-19, which sequentially undergoes all of the immunoglobulin gene rearrangement and expression events associated with the differentiation of pre-B cells to surface immunoglobulin-positive B lymphocytes. Analysis of the *in vitro* differentiation of 300-19 cells provides direct evidence for distinct differentiation phases of first V_H and subsequently V_L assembly during B-cell differentiation. Furthermore, these analyses suggest that the μ heavy chain, resulting from a productive V_HDJ_H rearrangement, has both a positive and a negative regulatory role in mediating this ordered differentiation process, that is, signalling the cessation of V_H gene assembly and simultaneously signalling the onset of V_L assembly.

The 300-19 Abelson murine leukaemia virus (A-MuLV)-transformed pre-B-cell line was derived from the adult bone marrow of NIH/Swiss mice^{3,6}. The original isolate of this line had DJ_H rearrangements on both J_H alleles and no light-chain gene rearrangements⁷, a molecular phenotype associated with the most immature pre-B-cell lines known^{3,6}. Both 300-19 DJ_H alleles are transcribed into $D\mu$ messenger RNA and one of these transcripts is translated into a $D\mu$ -chain, a truncated form of the μ heavy chain which contains D and μ constant region-derived sequence but no V_H -derived sequence⁷. Extensive subcloning has demonstrated that the normal low-level expression of $D\mu$ does not prevent additional J_H -specific rearrangements including frequent secondary D to J_H or V_H to DJ_H joinings^{7,8}. Approximately 20-30% of the V_H to DJ_H joinings in the 300-19 line are productive, generating progeny which accumulate high levels of normal μ -chains (see below). A few A-MuLV transformants which produced μ heavy chains at the time of isolation

have been observed to undergo V_κ assembly⁹⁻¹¹. However, no cell lines have been described previously which undergo both V_H and V_L assembly events. Because the 300-19 line forms productive V_HDJ_H rearrangements at high frequency, it seemed an ideal candidate to test for further differentiative capacity.

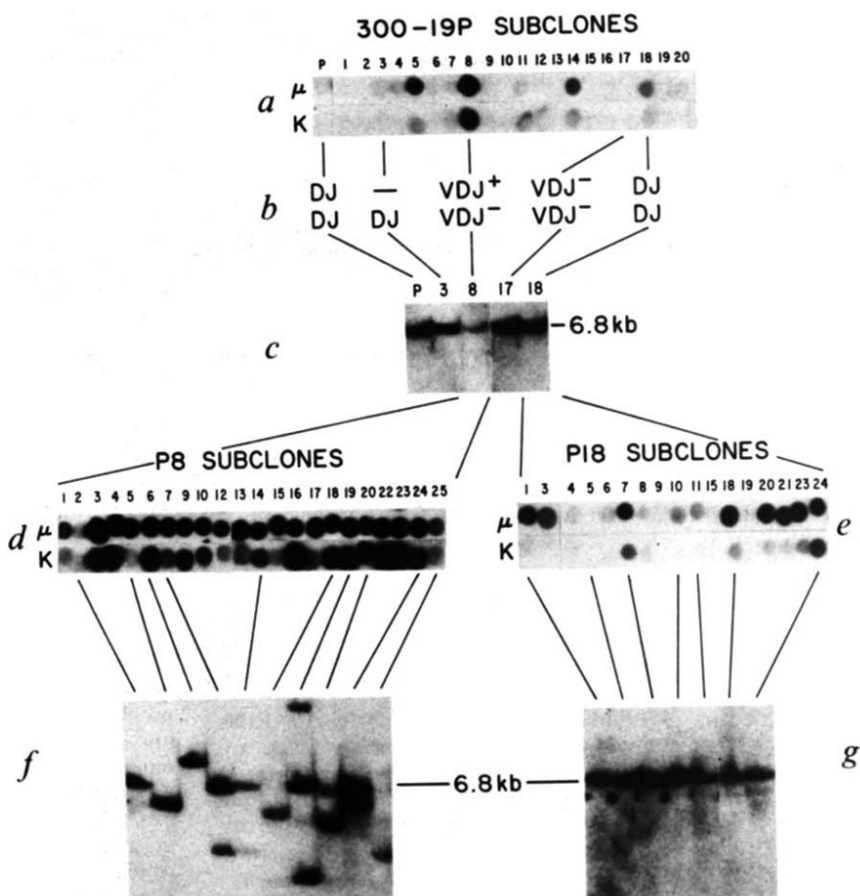
We have directly determined the rearrangement status of the heavy-chain alleles in the 300-19 parent line (P) and of those of numerous 300-19 subclones (a representative set is indicated in Fig. 1b); the types of rearrangements observed were DJ_H rearrangements (DJ), deletions of the J_H locus ($-$), and productive (VDJ^+) or non-productive (VDJ^-) rearrangements. To more easily assay for productive V_H and V_L assembly events in large numbers of 300-19 subclones (including events which were represented in a fraction of the population), we have devised a quick and sensitive screening assay for the presence of intracellular μ - and κ - and λ -chains. Briefly, the assay involves spotting equivalent amounts of lysate from appropriate cell lines onto nitrocellulose and then detecting bound immunoglobulin chains by a sandwich technique using a specific anti-mouse μ , κ or λ antiserum first, followed by a specific ¹²⁵I-labelled second antibody (see Fig. 1 legend). Conveniently, normal-sized μ -chains expressed in any 300-19 progeny which productively append a V_H segment to one of the parental DJ_H units can be distinguished from the $D\mu$ -chains expressed from one of the parental DJ_H alleles not only by their size difference⁷ but also by their expression level—which is, in general, much higher for the normal-sized μ -chain than the $D\mu$ -chain^{7,8}. For example, the low $D\mu$ expression of 300-19 parent cells is barely visible in our assay conditions (Fig. 1a), whereas most lines which have productive V_HDJ_H rearrangements give very strong signals (for example, the P8 line in Fig. 1). Furthermore, secondary subcloning demonstrated clearly that high-level μ expression in lines which by DNA blotting analyses appear to contain predominantly the parental DJ_H rearrangements (for example, lines P5 and P18 of, Fig. 1a, b) almost always resulted from the presence of a subpopulation of cells containing productive V_HDJ_H rearrangements (Fig. 1e; other data not shown). Thus, in the vast majority of clones which show clearly detectable μ -chain expression by this assay, at least some cells in the clonal population have formed productive V_HDJ_H rearrangements.

Analyses of light-chain expression revealed variable levels of κ -chains in many of the subclones but no λ expression. Furthermore, there was a strong correlation between μ -chain and κ light-chain expression in the various lines; κ -chains were found only in those lines that expressed normal μ -chains at intermediate to high levels (Fig. 1a). Thus, no κ -chains were detected in μ -negative lines which carried predominantly DJ_H alleles (for example, 300-19P, P3 and P18) or, even more significantly, in lines which had generated two non-productive V_HDJ_H rearrangements (for example, P17). However, we found very high-level κ expression in lines that had formed a productive V_HDJ_H rearrangement and which exhibited substantial μ -chain expression (for example, P8). Rearrangements of the J_κ locus in 300-19 subclones were analysed by probing a Southern blot of *Bam*HI/*Eco*RI double-digested genomic DNA with a J_κ -specific ³²P-labelled probe. In these assay conditions, a germline J_κ cluster is evident as a 6.8-kilobase(kb) hybridizing fragment¹⁰. Both the 300-19 parental population and all of the primary subclones contained only the germline fragment and no obviously rearranged bands (Fig. 1c; representative lines are shown). However, the germline band in DNA from the μ - and κ -positive P8 subclone was relatively faint, indicative of continuing κ -gene rearrangement. Thus, in the P8 subclone, the κ proteins detected appeared to have been generated from multiple cells in the population which harboured independent productive V_κ to J_κ rearrangements, any one of which was present in too low a molar ratio to be detected by the blotting assay. This assumption was proven by subcloning the P8 line. As expected, all the P8 subclones expressed μ -chains (Fig. 1d) and contained the same V_HDJ_H rearrangements as the parental line (not shown); however, nearly all these subclones also expressed κ -chains, some of them at high levels (Fig. 1d). In addition,

* Present address: Institute for Genetics, D5000 Cologne 41, FRG.

Fig. 1 Assembly and expression of V_H and V_L genes in the 300-19 cell line. *a*, Protein dot-blot assays (see below) of 300-19 cell lysates, indicating the presence of intracellular μ - and κ -chains in the 300-19 parent line (P) and in primary subclones (1-20). *b*, Rearrangement status of the two J_H alleles of 300-19 and representative subclones. The nature of each J_H -associated rearrangement was determined by DNA blotting assays using J_H -, D -, and V_H -specific probes as described previously^{6,7,16}. Whether a given V_HDJ_H rearrangement was productive (+) or non-productive (-) was determined by combined protein and DNA blotting assays as described previously⁷, or by direct nucleotide sequencing⁷. *c*, Rearrangement status of the J_κ alleles in 300-19 and representative subclones. Genomic DNA from the indicated lines was digested simultaneously with *Bam*HI and *Eco*RI, fractionated by electrophoresis through 1% agarose gels, transferred to nitrocellulose, and assayed for hybridization to the pRBJC κ probe as described in ref. 10. The 6.8-kb germline J_κ -containing fragment is indicated. *d, e*, Intracellular μ - and κ -chain expression in secondary subclones derived from subclone P8 (*d*) and P18 (*e*). *f, g*, Rearrangement status of the J_κ alleles in secondary subclones from P8 (*f*) and P18 (*g*); analyses were performed as described for *c*.

Methods. Primary or secondary subclones of 300-19 were obtained by subcloning the line or its primary isolates under limiting dilution conditions. Approximately 10^7 cells from each subclone were lysed with 200 μ l of phospholysis buffer⁷ and 3 μ l of each lysate spotted onto nitrocellulose. The filters were then treated with $6\times$ SSC, 70% ethanol, and incubated for 2-4 h in a 1% casein/phosphate-buffered saline (PBS) solution. Parallel filters were reacted separately with one of the three specific antisera: affinity-purified goat anti-mouse IgM; nitrophenol (NP)-coupled, monoclonal rat anti-mouse κ ; or the monoclonal anti-mouse λ antibody Ls136 (ref. 18). The filters were then washed three times with PBS and incubated with 125 I-labelled B1-8, a monoclonal anti-NP antibody (comprised of μ - and λ -chains) which could be bound by, or bind to, each of the three antisera. The detection limit of this specific sandwich assay was 100-1,000 pg ml⁻¹ of immunoglobulin chain.



almost all the subclones contained a rearrangement of at least one κ allele; and most of these rearrangements were of unique size, indicating that they resulted from independent events (Fig. 1f). The heterogeneity of κ -gene rearrangements in subclones containing a fixed, productive heavy-chain rearrangement clearly demonstrates that κ -chain production in μ -producing lines resulted from an onset of V_κ assembly after productive V_H rearrangement. In addition, similar analyses of several secondary and tertiary subclones which maintained the two parental DJ_H rearrangements, demonstrated that this sequential differentiation process is continuing in the 300-19 line. Thus, only those subclones which (assembled and) expressed significant levels of μ -chains underwent the rearrangement and expression of κ light-chain genes (for example, the P18 series; Fig. 1e, g). In agreement with the notion that light-chain gene assembly is also ordered^{13,10,12-14}, no evidence of λ light-chain gene assembly or expression was observed in any of the 300-19 subclonal series (data not shown).

A novel 300-19 subclone, p4-11, produced high levels of heavy chains of the $D\mu$ type, as evidenced both by the size of the chains (relative molecular mass 56,000) (Fig. 2a; the $D\mu$ -chains of the 300-19 parent line are included for comparison) and by the fact that the P4-11 line and its subclonal derivatives were directly demonstrated to maintain DJ_H rearrangements of both J_H alleles (not shown). Significantly, the P4-11 subclone expresses substantial levels of κ -chains by dot-blot analysis (not shown) which, on the basis of the subcloning and Southern blotting analyses described above, clearly resulted from a high level of V_κ to J_κ joining in the $D\mu$ -producing line (Fig. 2b). Thus, the $D\mu$ protein may contain the necessary components

to signal light-chain rearrangement, but in the vast majority of cases it is expressed at too low a level to effect such regulation. Furthermore, the maintenance of DJ_H rearrangements in all tested subclones of the P4-11 line (including those shown in Fig. 2b with independent J_κ rearrangements) suggests that high-level production of $D\mu$ chains might also be capable of mediating allelic exclusion.

In multiple independent primary, secondary and tertiary subcloning analyses, we have analysed hundreds of 300-19 subclones and have, with the one novel exception indicated above, yet to find a line which undergoes light-chain rearrangement and has not assembled and expressed a complete heavy-chain gene. Furthermore, all 300-19 subclones which do express complete heavy-chain genes (dozens of independent subclones) also show evidence of frequent κ light-chain gene assembly events. However, we have not observed light-chain rearrangement in several subclones which have assembled two non-productive V_HDJ_H rearrangements (for example, P17), indicating that V_L rearrangement is not associated with V_H assembly *per se*. Taken together, these findings argue strongly for separate phases of V_H and V_L assembly and further indicate that the production of μ heavy chains in some way mediates this transition. Such a role for the μ -chain is consistent with a model which postulates that the regulation of all aspects of V-gene assembly (for example, allelic exclusion, order) is mediated by the relative accessibility of the component V_H and V_L gene segments to a common recombinase¹⁵. Thus, the production of a μ -chain could serve the dual function of signalling the 'closing' of the previously accessible V_H locus (effecting allelic exclusion) and the 'opening' of a previously non-accessible J_L locus (effecting

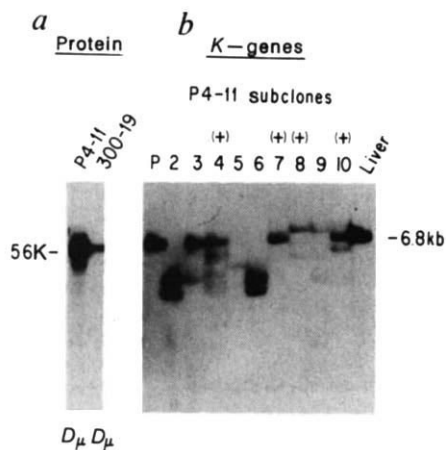


Fig. 2 High-level expression of $D\mu$ -chains is associated with $V\kappa$ assembly. *a*, $D\mu$ expression. Approximately 10^7 300-19 or subclone P4-11 cells were lysed, fractionated by polyacrylamide gel electrophoresis, electrotransferred to a nitrocellulose filter, and the bound μ -chains detected by a sandwich technique using goat anti-IgM and ^{125}I -labelled monoclonal IgM antibody B1-8 (see ref. 7 for details). *b*, Genomic DNA from the P4-11 line (lane P), various P4-11 secondary subclones (lanes 2-10) and mouse liver (liver) was assayed for $J\kappa$ rearrangement as described in Fig. 1 legend.

ordered rearrangement). A clue to some of the necessary molecular determinants of this putative signal may come from the observation that high-level expression of a truncated heavy-chain protein containing just D and $C\mu$ portions ($D\mu$ protein) may also signal the onset of V_L assembly and the cessation of V_H assembly.

Several 300-19 subclones which produce both μ - and κ -chains contain a large percentage of cells (30%) that express these chains on their surface in the form of IgM; in contrast, the parental line or μ -only intermediates do not express surface immunoglobulin (data not shown). The acquisition of surface IgM by the μ - and κ -producing subclones was often accompanied by the appearance of additional surface markers diagnostic of the B-cell stage of differentiation, including surface IgD (unpublished results). Thus, the 300-19 line represents, to our knowledge, the first permanent cell line of any type that clearly undergoes all of the sequential gene reorganization and expression events which lead to the surface IgM-positive stage of B-lymphocyte differentiation. Previously characterized A-MuLV transformants which were shown to undergo V_H to DJ_H rearrangement did not appear to go on to the V_L assembly stage. However, these lines, which were derived from the fetal liver of BALB/c mice, rearranged a highly restricted set of V_H gene segments¹⁶ and usually generated V_HDJ_H -containing progeny in which these rearrangements were non-productive¹⁷, suggesting a detrimental effect of the expression of the frequently used V_H gene segments. The 300-19 line, on the other hand, uses a very different set of V_H gene segments to form V_HDJ_H rearrangements⁸ and generates, at high frequency, progeny which have formed productive rearrangements (see above). Taken together, our observations suggest that the relative ability of these lines to differentiate to the V_L assembly stage may be a function of their inherent capacity to generate progeny which have assembled and expressed productive V_HDJ_H rearrangements, rather than some consequence of the A-MuLV transformation event *per se*. The *in vitro* differentiation of the 300-19 line appears to occur spontaneously and rapidly with no additional stimulant needed beyond that potentially provided by components of the growth medium. This portion of the normal B-cell differentiation pathway probably also occurs in the spontaneous and autoregulatory manner observed in 300-19 cells, with the product of one differentiation stage signalling the onset of the next stage.

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T-cell clones specific for myelin basic protein induce chronic relapsing paralysis and demyelination

Scott Zamvil*, Patricia Nelson†, Jacqueline Trotter*, Dennis Mitchell*, Robert Knobler‡, Robert Fritz§ & Lawrence Steinman*

* Departments of Pediatrics and Neurology, Stanford University School of Medicine, Stanford, California 94305, USA

† Carcinex, Inc., Burlingame, California 94010, USA

‡ Department of Neurology, Jefferson Medical College, Philadelphia, Pennsylvania 19107, USA

§ Department of Microbiology, Emory University Medical School, Atlanta, Georgia 30322, USA

Experimental allergic encephalomyelitis (EAE) serves as a model for autoimmune diseases mediated by T lymphocytes^{1,2}. Following sensitization to rat, mouse or guinea pig myelin basic protein (MBP) in complete Freund's adjuvant, inbred mouse strains PL/J ($H-2^b$), SJL/J ($H-2^d$) and (PL/J × SJL/J) F_1 (PLSJ) F_1 develop EAE^{3,4}. Whereas sensitization to the N-terminal 37 amino-acid peptide of rat or guinea pig MBP [MBP(1-37)] induces EAE in PL/J mice, immunization to the C-terminal peptide (89-169) leads to EAE in SJL/J mice^{4,5}. The immune response to MBP in (PLSJ) F_1 mice is not co-dominant; sensitization to the N-terminal peptide induces EAE, while sensitization to the C-terminal peptide does not^{3,4}. We have generated MBP-specific T-cell clones restricted to class II (Ia) antigens of the major histocompatibility complex (MHC) from PL/J and (PLSJ) F_1 mice following sensitization to rat MBP. Two such I-A^b-restricted T-cell clones that proliferate in response to the encephalitogenic N-terminal MBP peptide and recognize a shared determinant with mouse (self) MBP cause paralysis in 100% of (PLSJ) F_1 mice tested. Paralysis is induced even when recipients are injected with as few as 1×10^5 cloned T cells. Relapsing paralysis followed in two-thirds of the recipients after recovery from acute paralysis, whereas one-third developed chronic persistent paralysis, a form of EAE not usually seen. Histopathology revealed intense perivascular inflammation, demyelination and remyelination within the central nervous system of paralysed mice. The experimental disease induced with these clones shares important features with human demyelinating diseases such as multiple sclerosis. This is the first demonstration that T-cell clones that respond to a defined self-antigen can induce clinical and histological autoimmune disease.

T lymphocytes sensitized to MBP can cause clinical and histological EAE when adoptively transferred to naive

Table 1 Response of T-cell clones to MBP

Encephalitogenic clones	Antigen-presenting cells	Response to MBP (mean c.p.m. ³ H-thymidine incorporation)			
		No antigen	Rat MBP	Bovine MBP	Mouse MBP
Clone PJR-25	PL/J	276	88,341	27,859	73,421
	SJL/J	319	266	145	292
	(PLSJ) _F ₁	99	76,726	4,170	22,574
Clone F1-12	PL/J	530	54,743	6,013	16,038
	SJL/J	1,659	1,663	2,150	1,964
	(PLSJ) _F ₁	530	42,666	2,712	5,358
Non-encephalitogenic clones					
Clone F1-13	PL/J	281	666	314	355
	SJL/J	766	37,094	447	262
	(PLSJ) _F ₁	174	15,544	166	230
Clone F1-15	PL/J	176	288	ND	ND
	SJL/J	2,110	2,404	ND	ND
	(PLSJ) _F ₁	1,789	239,244	2,169	2,924
Clone F1-16	PL/J	73	279	ND	ND
	SJL/J	152	216	ND	ND
	(PLSJ) _F ₁	126	35,173	138	206

Proliferative T-cell lines specific for MBP were generated from PL/J and (PLSJ)_F₁ mice following protocols previously described²³. Five mice per group of each strain were immunized subcutaneously at the base of the tail with 200 µg rat MBP emulsified in complete Freund's adjuvant (CFA). Seven days later, draining inguinal and para-aortic lymph nodes were removed, cells were suspended in media and cultured in 24-well dishes (Costar, 3524) at 6×10^5 cells per well with 100 µg ml⁻¹ rat MBP. Eight days later, cells were collected, washed twice and 5×10^5 viable cells were transferred to 25-cm² tissue culture flasks (Corning 25100). These cells were stimulated with 3×10^7 γ-irradiated (3,300 rad) APC and 100 µg ml⁻¹ MBP. Twelve days after the previous stimulation, viable resting T cells were separated by centrifugation over a Ficoll gradient. At this time T cells were cloned by limiting dilution in 96-well flat-bottom microtitre plates (Linbro, 76-003-05) at 0.3 cells per well with 5×10^5 syngeneic APC, 100 µg ml⁻¹ rat MBP and 10% supernatant from concanavalin A-stimulated rat spleen cells (CAS)²³. After 12 days, cell growth was observed in only 8–10% of the wells. Cells from individual wells were expanded in 24-well Costar plates in the same manner with 5% CAS and eventually transferred to 25-cm² tissue culture flasks. Then 5×10^5 cloned T cells were routinely stimulated every 12–14 days without CAS. Clone PJR-25 was subcloned by sorting at 1 cell per well using FACS. Complete culture media consisted of RPMI 1640 (Gibco) supplemented with 10% fetal calf serum (M.A. Bioproducts), 5×10^{-5} M 2-mercaptoethanol, 2 mM glutamine, 100 U ml⁻¹ penicillin and 100 µg ml⁻¹ streptomycin. To assay for proliferative response to rat, bovine or mouse MBP, 10^4 T cells were cultured with 5×10^5 irradiated APC from PL/J, SJL/J or (PLSJ)_F₁ mice in 0.2 ml culture media in 96-well flat-bottomed microtitre plates. MBP from each species was isolated as described previously²⁴. Each clone was tested with and without rat MBP. Cultures were pulsed using 1 µCi ³H-thymidine at 48 h and collected 16 hours later. The mean c.p.m. of thymidine incorporation was calculated for triplicate cultures. The standard deviations from replicate cultures were within 10% of the mean value. ND, not done.

recipients^{6–10}. The T cells that are transferred in these experimental systems are heterogeneous polyclonal populations capable of responding to various antigenic determinants on MBP⁹. It is important to define precisely which T cells are involved in induction of EAE, because many cells contained in bulk T-cell cultures^{6,7}, or even long-term T-cell lines^{8–10}, may not be involved in the induction of autoimmunity. In an investigation of the properties of the cells participating in the pathogenesis of EAE, examining cloned populations of T cells that react to MBP is advantageous. We established proliferative T-cell lines specific for MBP in PL/J and (PLSJ)_F₁ mice following immunization with rat MBP. Clones were then derived from these T-cell lines. The response of the clones to mouse (self) MBP and peptides derived from MBP was analysed. Since T cells recognize antigen in association with class II MHC antigens, these clones were further characterized on the basis of their pattern of restriction to I-A or I-E molecules. The clones were then tested for their ability to induce EAE in (PLSJ)_F₁ mice. The properties of two encephalitogenic clones, PJR-25 derived from PL/J mice and F1-12 derived from (PLSJ)_F₁ mice, are described here. The characteristics of three MBP-specific non-encephalitogenic 'control' clones, F1-13, F1-15 and F1-16, are also presented.

Clones PJR-25 and F1-12 proliferate in response to rat, bovine or mouse MBP, but only in association with H-2^u MHC molecules expressed on PL/J and (PLSJ)_F₁ antigen-presenting cells (APC) (Table 1). Neither clone is alloreactive for H-2^s or

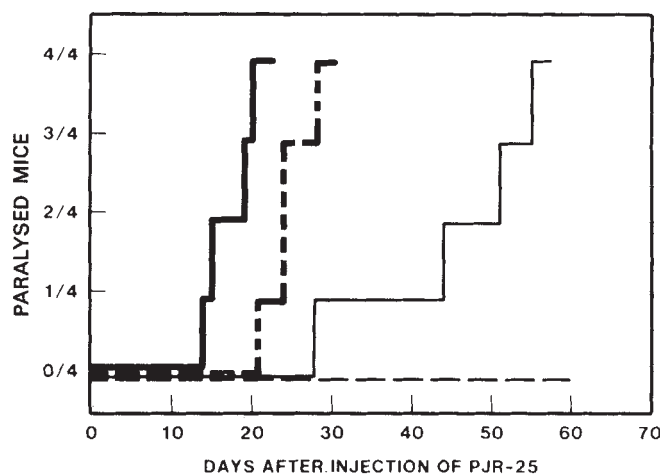


Fig. 1 Onset of paralysis in (PLSJ)_F₁ mice after injection of MBP-specific T-cell clone PJR-25.

Methods. (PLSJ)_F₁ mice were injected intravenously (i.v.) with 1×10^6 (thick solid line), 5×10^5 (thick broken line) or 1×10^5 (thin solid line) PJR-25 cells, or 5×10^6 control T-cell clones specific for MBP, which do not proliferate to mouse MBP (thin broken line). Fourteen days after stimulation with rat MBP and irradiated APCs, viable T cells were separated by centrifugation through a Ficoll gradient. These cells were then stimulated for 24 h in complete media containing 10% CAS (see Table 1 legend) in the absence of APC. Recipient mice were given low-dose whole-body irradiation (350 rad) and 10^{10} heat-inactivated *B. pertussis* i.v. prior to T-cell injection, and a second *B. pertussis* injection was given ~48 h after injection of PJR-25 cells. Onset of paralysis is defined as the first signs of hind-limb paraparesis or paraplegia and loss of tail tone.

H-2^{u/s} F₁ antigens expressed on (PLSJ)_F₁ APC. Both PJR-25 and F1-12 respond to peptides composed of guinea pig and bovine MBP(1–37) (Table 2). Rat and guinea pig MBP have identical amino-acid sequences for residues 1–37, and differ from mouse MBP at only two residues. Mouse MBP is missing His 10 and Gly 11 (ref. 11). Bovine MBP(1–37) also has this deletion, but differs from rat, guinea pig and mouse MBP at residues 2 and 17 (see Table 2 legend).

In PL/J and (PLSJ)_F₁ mice, two similar but separately encoded Ia antigens, I-A and I-E, can be expressed. Whether antigen recognition occurs in association with a particular Ia complex can be determined by using monoclonal antibodies that recognize only specific I-A or I-E gene products^{12,13}. These monoclonal antibodies bind to I-A or I-E molecules on APC and block T-cell recognition, thus inhibiting T-cell proliferation. Using this approach, we found that PJR-25 and F1-12 are both I-A^u-restricted (Table 3).

Clones PJR-25 and F1-12 were considered good candidates to test *in vivo* for induction of EAE because each clone recognizes an epitope within the encephalitogenic N-terminal peptide that is shared with mouse (self) MBP. We predicted that MBP-specific T-cell clones that do not respond to mouse MBP *in vitro* would be unlikely to cause EAE in mice. Clone PJR-25, which has the phenotype of a T-helper cell (Ly1⁺, Lyt 2⁺, L3T4⁺) as determined by fluorescent-activated cell sorter (FACS) analysis (data not shown), was the first clone tested *in vivo*.

In five consecutive experiments, 100% of (PLSJ)_F₁ mice developed paralysis after a single injection of PJR-25 (Fig. 1). Even when injected with as few as 10^5 cells, the smallest number yet tested, all of four mice developed paralysis. The onset of paralysis is, however, dependent on the number of PJR-25 cells injected. With greater numbers of cells, clinical signs appear earlier (Fig. 1) and death is more likely. Of 12 mice injected with 5×10^6 PJR-25 cells, all developed acute EAE within 10–14 days (data not shown). Eight mice died 1–5 days after onset of paralysis, and the other four mice were used for histological studies when found moribund.

After an injection of 10^6 or 5×10^5 PJR-25 cells, some mice

Table 2 Response of T-cell clones to peptide fragments of MBP (mean c.p.m. ^3H -thymidine incorporation)

Encephalitogenic clones	No antigen	Rat MBP	Guinea pig MBP	Guinea pig MBP(1-37)	Bovine MBP(1-37)	Bovine MBP(89-169)
PJR-25	143	117,592	83,489	108,853	39,715	392
F1-12	125	48,326	19,223	53,839	11,125	126
Non-encephalitogenic control clones						
F1-13	55	32,779	53	37	42	52
F1-15	50	36,580	39,011	43,108	32	26
F1-16	68	74,286	83,687	95,650	133	247

All MBP peptides are products of pepsin cleavage from either intact guinea pig MBP or bovine MBP. These peptides have been isolated and purified as previously described³⁻⁵. Guinea pig MBP(1-37) has the identical sequence to rat MBP in this N-terminal region and bovine MBP(89-169) shares the same amino-acid sequence as large rat MBP(89-169)¹¹. Bovine MBP(1-37) differs from the rat and guinea pig MBP(1-37) sequence at residue 2, where Ala replaces Ser, and residue 17, where Ser replaces Thr. Bovine MBP has a deletion of the His 10 and Gly 11 residues. Although these clones do not proliferate to bovine MBP(89-169), this peptide does not suppress the proliferation to either MBP(1-37) (not shown). MBP(89-169) has been found to stimulate certain MBP-specific proliferative T-cell clones derived from SJL/J mice⁹. All peptides were added at initiation of the cultures to give a final concentration of 50 $\mu\text{g ml}^{-1}$. Intact proteins were also added but at a concentration of 100 $\mu\text{g ml}^{-1}$. Syngeneic irradiated APC were used in all cultures (see Table 1). Proliferative responses were determined as described in Table 1 legend.

Table 3 Pattern of I-region restriction of T-cell clones (mean c.p.m. ^3H -thymidine incorporation)

Encephalitogenic clones	No antigen	Rat MBP + anti-I-A $_{\beta}$ ^{u,s} (10-2.16)	Anti-I-A $_{\beta}$ ^u (40 M)	Anti-I-E $_{\alpha}$ ^u (14-4.4)	Anti-I-E $_{\alpha}$ ^{s/u} (Y-17)
PJR-25	213	125,562	7,018	5,181	108,853
F1-12	125	48,326	8,828	2,474	63,078
Non-encephalitogenic control clones					
F1-13	361	33,002	28,025	27,303	38,253
F1-15	394	99,266	345	364	102,890
F1-16	68	69,552	133	185	65,603

All monoclonal antibodies have been described previously²⁵⁻²⁸. Antibody 10-2.16 binds determinants Ia.17 on certain I-A $_{\beta}$ chains including A $_{\beta}$ ^s and A $_{\beta}$ ^u (ref. 25). Antibody 40 M binds Ia.1, a determinant on I-A $_{\beta}$ ^u, but not on I-A $_{\beta}$ ^s (ref. 26). Antibody 14-4.4 binds determinant Ia.7 expressed on certain E $_{\alpha}$ chains including E $_{\alpha}$ ^u (ref. 27). Antibody Y-17 binds a determinant, Ia.m44, on certain hybrid I-E molecules including E $_{\alpha}$ ^uE $_{\beta}$ ^s (ref. 28). In these blocking studies 1 μg of each antibody was added at the beginning of culture to those wells containing cloned T cells, syngeneic APC and rat MBP. 10-2.16, 14-4.4 and Y-17 were provided by Dr P. P. Jones (Stanford University). Proliferative responses were determined in the same manner as described in Table 1 legend.

have developed acute paralysis followed by death, as was seen when 5×10^6 cells were injected. Many, however, develop chronic relapsing paralysis, and a small number develop chronic unremitting paralysis, a form not usually observed. In three experiments in which a total of 28 mice were injected with either 1×10^6 or 5×10^5 PJR-25 cells, 13 mice died 3-9 days following the onset of paralysis. Eleven of the 15 mice that survived the initial onset of paralysis developed hind-limb paraplegia and complete loss of tail tone, which lasted 6-10 days and then improved with no other observable signs of paralysis. These 11 mice relapsed 10-25 days later, developing at least hind-limb paraparesis and usually complete paraplegia for 6-20 days duration. Of these 11 mice, 8 underwent a second remission, with 3 of those relapsing for a second time (20 days later). The other 3 mice from the 11 remained chronically paralysed (>40 days). The remaining 4 of the 15 mice that survived the initial onset of paralysis were chronically paralysed (either severe paraparesis or complete paraplegia) for more than 80 days without signs of deterioration or remission. This chronic persistent form of paralysis is unusual in mice with EAE.

Classic histological features of EAE, including perivascular infiltrates in the central nervous system and meningeal inflammation, were observed (Fig. 2). Demyelination and remyelination accompanied the cellular inflammation in mice with both chronic relapsing and chronic unremitting paralysis (Fig. 2).

A subclone of PJR-25 was also observed to cause paralysis in mice. This subclone, called PJr-25, was derived by sorting the parent clone at one cell per well using FACS analysis. When injected with 1×10^6 PJr-25 cells, all of four (PLSJ) F_1 recipient mice developed clinical EAE with chronic paralysis. Two of these four mice relapsed. The encephalitogenic potential of this clone was not diminished by subcloning or by continuous culture *in vitro* for more than 10 months.

T-cell clone F1-12 was also tested *in vivo*. This clone, derived from (PLSJ) F_1 mice, has a similar MBP recognition pattern as PJR-25. It responds to the encephalitogenic N-terminal peptide (Table 2), recognizes a conserved epitope with mouse MBP (Table 1), and is also I-A $_{\beta}$ -restricted (Table 3). When tested *in vivo*, paralysis was observed in four of four (PLSJ) F_1 recipient mice. These mice developed paraparesis and, in two cases, the paraparesis evolved to monoparesis. In one case a mouse developed paraparesis followed 14 days later by right leg monoparesis. Ten days later paraparesis recurred and 40 days later right leg monoparesis developed a second time.

MBP-specific T-cell clones that respond to rat MBP but not to mouse MBP were administered to (PLSJ) F_1 mice in the same manner as the encephalitogenic clones PJR-25, PJr-25 and F1-12. Three different control clones, F1-13, F1-15 and F1-16, were injected (5×10^6 cells) into (PLSJ) F_1 recipients. None out of 21 of these recipient mice developed clinical paralysis (see Fig. 1 legend). Demyelination was not observed in tissue sections from mice given control clones. These T-cell clones were derived from (PLSJ) F_1 mice immunized with rat MBP. One of these clones, F1-13, responds to rat MBP only (Table 1), and solely in association with SJL/J APC. The other two clones, F1-15 and F1-16, recognize a determinant within the encephalitogenic N-terminal peptide of rat and guinea pig MBP that is not shared by mouse MBP (Table 2). This determinant probably includes His 10 and Gly 11, present in guinea pig MBP and rat MBP, but deleted in mouse MBP as this is the only difference in amino acids 1-37 between mouse MBP and rat or guinea pig MBP. Both F1-15 and F1-16 respond to rat MBP only in association with (PLSJ) F_1 hybrid APC, not parental APC (Table 1). Monoclonal antibodies to I-A $_{\beta}$ ^u block proliferation of these clones to rat MBP. Clones F1-15 and F1-16 are thus restricted to I-A $_{\beta}$ ^sA $_{\beta}$ ^s (Table 3).

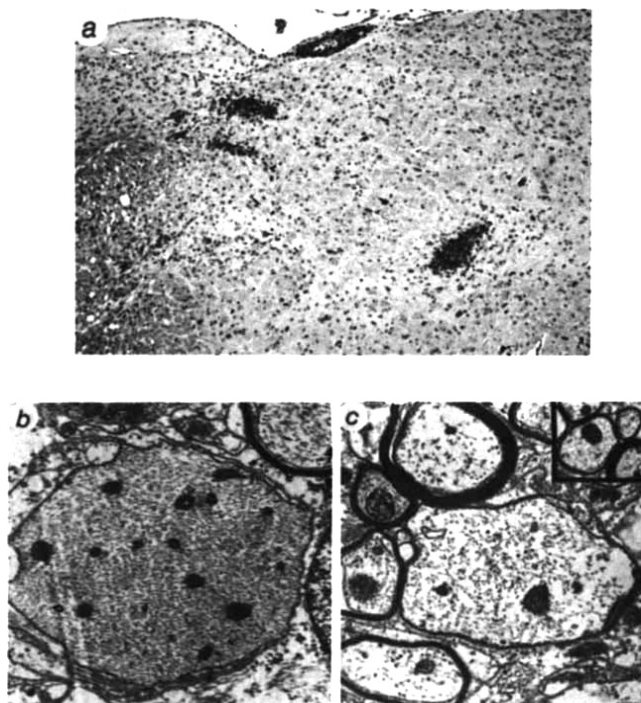


Fig. 2 *a*, Histological evidence of EAE. Representative perivascular cuffs from cortex of mouse with paraparesis 25 days after receiving PJR-25, 5×10^5 cells. $\times 150$, haematoxylin and eosin stain. *b*, A completely demyelinated axon, demonstrating primary demyelination in a mouse injected with MBP-specific T-cell clone PJR-25. This mouse was killed during a relapse, 45 days after initial signs of paralysis. A portion of a remyelinated axon is present in the upper right corner. $\times 17,500$. *c*, A partially remyelinated axon is evident in the centre of the field, which is surrounded by several remyelinated axons. The inset in the upper right corner shows several additional remyelinated axons, characterized by a thin myelin sheath around the axonal profile. A more normal axonal sheath profile is present in the lower right corner of the inset. $\times 17,500$.

The failure of any of the three control clones to induce EAE mitigates against passive transfer of MBP as a mechanism for EAE induction. These clones all proliferate in response to rat MBP as well as to PJR-25 or F1-12. Thus, if any trace amount of rat MBP is passively transferred with PJR-25, PJR-25 or F1-12, similar amounts are probably transferred with the control clones handled in the same manner.

As in other systems in which murine T-cell lines have been used to induce EAE^{8,9,14}, we have found that low-dose irradiation of the recipients (see Fig. 1 legend) facilitates induction of severe clinical EAE. Thus, all of eight (PLSJ)F₁ mice receiving 1×10^6 PJR-25 T cells with radiation (350 R) but without *Bordetella pertussis* developed relapsing paralysis, while none of eight mice without irradiation that received *B. pertussis* intravenously developed EAE. One of eight mice developed EAE without irradiation or *B. pertussis*. Preliminary results revealed that *in vivo* administration of recombinant human interleukin-2 (provided by Cetus) permitted induction of EAE with clone PJR-25 without the need for either radiation or *B. pertussis* (S.Z. *et al.*, in preparation).

These experiments demonstrate for the first time that EAE can be induced with individual T-cell clones. Class II (I-A)-restricted T cells bearing the L3T4 phenotype characteristic of helper-inducer cells, which recognize the N-terminal peptide of MBP, are highly encephalitogenic. We have shown previously that EAE can be prevented and that progressive paralysis can be reversed with *in vivo* administration of either anti-I-A or anti-L3T4 antibody¹⁵⁻¹⁷. These antibodies may be effective through blockade of activation of T cells restricted to class II MHC molecules¹⁵⁻¹⁸. It is intriguing that astrocytes isolated

from the central nervous system express class II MHC antigens, when cultured *in vitro* with T-cell lines specific for MBP, and are capable of presenting MBP to these T-cell lines^{19,20}. Ia antigens can be demonstrated on endothelial cells in the central nervous system early in the development of EAE²¹. Thus, it is likely that these T-cell clones recognize MBP in association with Ia antigens present in the brain and spinal cord.

These T-cell clones induce a variety of clinical states, including acute fulminant paralysis, relapsing-remitting paralysis and chronic persistent paralysis. It is clear that a single cloned T-cell population can induce relapsing paralysis. The number of cloned T cells that are administered is a critical factor in determining the clinical course. Whether recurrent paralysis and demyelination in part results from sensitization to MBP plus lipids—a question raised by others⁷—can now be excluded by the finding that cloned T cells reactive to MBP peptides induce relapses and demyelination.

The availability of T-cell clones specific for defined regions of the MBP molecule that mediate EAE, the archetypal model for autoimmunity induced with T cells, provides several opportunities to study the pathophysiology of this disease. Because clinical relapses and demyelination are induced with these clones, this model disease shares important features with human demyelinating diseases such as multiple sclerosis. These T-cell clones provide decisive advantages for studying such questions as the migration of T cells to the central nervous system in disease²², and the molecular biology of the T-cell receptors for the encephalitogenic epitope of MBP. Using smaller peptides, we are currently defining the region within MBP (1-37) that is recognized by disease-inducing clones. If encephalitogenic T cells responding to the N-terminus of MBP recognize the same epitope, they possibly share structural similarities in their MBP-specific T-cell receptors. If so, the development of clonotypic antibodies against MBP-specific T-cell clones can be tested in this system to determine whether they could be beneficial in the therapy of T cell-mediated autoimmune diseases. Finally, because these clones induce relapsing disease, the regulatory mechanisms leading to relapse and remission can be studied following a single injection of a clonally derived population.

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Binding of immunogenic peptides to Ia histocompatibility molecules

Bruce P. Babbitt*, Paul M. Allen*, Gary Matsueda†, Edgar Haber† & Emil R. Unanue*

Department of Pathology, Harvard Medical School, Boston, Massachusetts 02115, USA

* Washington University School of Medicine, St Louis, Missouri 63110, USA

† Cardiac Unit, Massachusetts General Hospital, Boston, Massachusetts, 02114, USA

Most cellular interactions essential for the development of an immune response involve the membrane glycoproteins encoded in the major histocompatibility gene complex¹⁻³. The products of the I region, the class II histocompatibility molecules (Ia molecules), are essential for accessory cells such as macrophages to present polypeptide antigens to helper T cells. This interaction, antigen presentation, is needed for T-cell recognition of the antigen and its consequent activation. How the Ia molecules regulate the immune response during antigen presentation is not known, although it is commonly thought to result from their association with the presented antigen^{1,4,5}. Recent studies, including the elucidation of the structure of the T-cell receptor, favour recognition of a single structure, an antigen-Ia complex⁶⁻⁸. Here we report attempts to determine whether purified Ia glycoproteins have an affinity for polypeptide antigens presented by intact cells in an Ia-restricted manner. We first identified the epitope of a peptide antigen involved in presentation⁹. Several laboratories have shown that globular proteins are altered (processed) in intracellular vesicles of the antigen-presenting cell before antigen presentation¹⁰⁻¹². A major component of the T-cell response is directed toward determinants found in the unfolded or denatured molecule, and our laboratory has shown that the determinant of the hen-egg lysozyme protein (HEL), presented in H-2^k mice to T cells, is a sequence of only 10 amino acids⁹. This portion resides in an area of the native molecule partially buried inside the molecule, in a β -sheet conformation. To be presented, intact or native HEL must first be processed in acidic intracellular vesicles¹². Having isolated the peptide responsible for T-cell recognition of HEL, we sought a physical association of this peptide with purified, detergent-solubilized I-A^k molecules from B-hybridoma cells. We have found such an association, which may explain the role of the Ia glycoproteins in cellular interactions.

If antigen presentation involves a direct complexing of a peptide to the I-A molecule, we reasoned that binding can be measured directly in detergent micelles. We accomplished this by purifying I-A^k and I-A^d glycoproteins on a large scale and examining the binding of a peptide antigen to each of them by equilibrium dialysis. As antigen we selected a peptide of lysozyme, HEL(46-61), that is immunogenic in mice of the H-2^k but not of the H-2^d haplotype. We had previously developed a panel of T-cell hybridomas in mice of the H-2^k haplotype that recognize the peptide HEL(46-61). HEL(46-61) was synthesized by the solid-phase method of Merrifield and purified using reverse-phase HPLC⁹. The compound 7-fluoro-4-nitrobenzo-2-oxa-1,3-diazole (NBD-F) was then covalently bound to the HEL(46-61). The resultant fluorescently labelled polypeptide antigen was separated from residual HEL(46-61) using HPLC, and found to be derivatized at its amino terminus by measurement of its ultraviolet and visible absorption spectra¹³. NBD-HEL(46-61) was still strongly immunogenic compared with native HEL(46-61) (Fig. 1). For example, the amount of NBD-HEL(46-61) presented by the B-hybridoma line TA3 required for half-maximal stimulation of interleukin-2 (IL-2) production by a T-cell clone was apparently six- to eightfold less than the amount of native HEL(46-61) required for a similar response. Consequently, we could use this functional well-defined NBD-HEL(46-61) probe to measure the binding affinity of the peptide

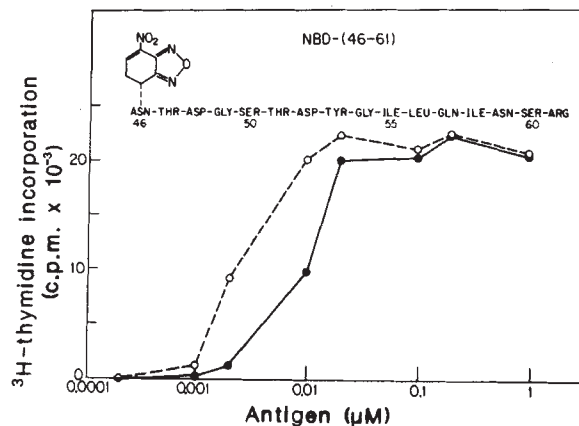


Fig. 1 Response of 3A9 T-cell hybridoma to either native HEL(46-41) (●) or NBD-HEL(46-61) (○). TA3 B-hybridomas were used as antigen-presenting cells and 10⁴ TA3 cells incubated in 200 μ l in 96-well Costar dishes with 10⁵ 3A9 cells and the indicated amounts of peptide. After 24 h of culture, supernatants were removed and assayed for IL-2 activity by the incorporation of ³H-thymidine into the IL-2-dependent cytotoxic T-lymphocyte cell. The values represent the arithmetic mean of triplicate culture wells; standard deviations were <20% of the mean. Previous studies indicated that 3A9 responds only to I-A^k macrophages pulsed with HEL¹². The 3A9 T-cell hybridomas, derived in our laboratory from CBA/J mice immunized with HEL, were previously shown to react with native HEL after processing, or with HEL(46-61)²⁵. The structure of NBD-(46-61) is also shown.

for purified I-A in detergent. We purified I-A^k and I-A^d (ref. 14) molecules from the TA3 line (an I-A^{d/k}-bearing hybridoma active in antigen presentation)¹⁵ and incubated them with NBD-HEL(46-61), measuring their association by equilibrium dialysis.

NBD-HEL(46-61) could bind to the I-A^k polypeptide but not to an excess of I-A^d (Figs 2, 3), establishing that the binding was haplotype-specific. In a control experiment, NBD-HEL(46-61) did not bind significantly to excess amounts of an unrelated membrane protein, glycoporphin (Fig. 3). The binding to I-A^k of the NBD-HEL(46-61) was saturable (Fig. 2), exhibiting a dissociation constant (K_D) of $\sim 2 \mu$ M (we have performed four separate experiments with values ranging from 1.4 μ M to 4.8 μ M with a mean of 2.8 μ M.) From the x-axis intercept of the Scatchard plot we have calculated a molar ratio at equilibrium binding between I-A^k and NBD-HEL(46-61) of 0.82. Finally, the binding of NBD-HEL(46-61) to I-A^k was strongly inhibited by native HEL(46-61), indicating that the binding is specific (Fig. 3). A synthetic analogue of HEL(46-61) (see Fig. 3 legend) that is not presented by TA3 cells to T-cell hybridomas did not exhibit any appreciable competition with NBD-HEL(46-61) for binding to I-A^k. This peptide contained conservative substitutions at the eight amino acids to the carboxy side of Tyr 53 (therefore, overall peptide length, hydrophobicity and β -structure propensity are similar). Furthermore, the inability of the analogue to inhibit NBD-HEL(46-61) binding indicates that the interaction of I-A^k with the peptide antigen is sensitive to the amino-acid sequence of the carboxy portion of the molecule. We are currently testing a panel of HEL(46-61) homologues and analogues of known immunogenicity for their ability to compete with NBD-HEL(46-61) for binding to I-A^k; this should establish whether a strong relationship exists between the binding to purified I-A^k and the immunogenicity of a peptide.

Our results are compatible with a model in which the Ia molecule binds a peptide sequence and thus creates the structural determinant recognized by T-helper cells. Perhaps the affinity of the interaction between Ia and peptide would dictate the *I*r gene responder status. Indeed, we have detected rather strong and specific binding to I-A^k, the responder haplotype, but no binding to I-A^d, the non-responder, nor to glycoporphin,

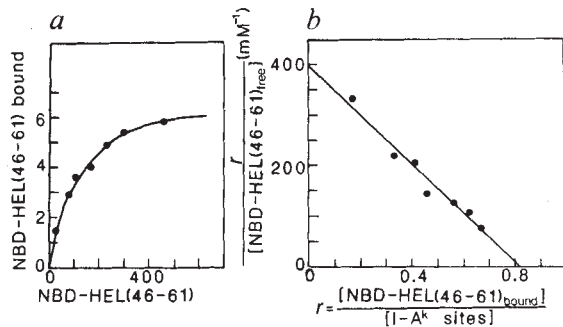


Fig. 2 *a*, Saturation binding curve and *b*, Scatchard plot of binding data, obtained by equilibrium dialysis for the binding of NBD-HEL(46-61) to I-A^k in 0.25% Triton X-100; $K_d = 2.0 \mu\text{M}$. **Methods.** Binding was performed at 37 °C for 72 h using an I-A^k preparation obtained from TA3 B-hybridoma cells. Large-scale purification by affinity chromatography using the anti-I-A^k monoclonal antibody 10-2.16, coupled to cyanogen bromide (CNBr)-activated Sepharose 4B (ref. 14) was performed using $\sim 10^{11}$ TA3 cells. Cells were washed in phosphate-buffered saline (PBS) at pH 7.4 and plasma membranes obtained by nitrogen cavitation at 400 p.s.i. for 5 min, followed by centrifugation at 18,500 r.p.m. in a Sorvall SS-34 rotor for 30 min. Plasma membranes were washed in 0.5 M NaCl and 5 mM EDTA to remove peripheral membrane proteins and contaminating actin and myosin. Finally, plasma membranes were solubilized in 0.5% Triton X-100 and passed through a 12-ml Sepharose 4B column coupled with purified 10-2.16 (24 mg purified IgG had been coupled to 3.5 g CNBr-activated Sepharose 4B). I-A^k was eluted from the column in 0.5% deoxycholate and quantitated using the fluorescamine assay. I-A^d was purified from solubilized TA3 plasma membrane material that failed to bind to the 10-2.16-coupled Sepharose 4B column using the anti-I-A^d monoclonal antibody MKD6 coupled to CNBr-activated Sepharose 4B by a procedure identical to that for I-A^k purification. All purification steps were performed at 4 °C in the presence of 5 mM EDTA, 0.2 mM phenylmethylsulphonyl fluoride and 5 mM iodoacetamide. SDS-polyacrylamide gel electrophoresis of the I-A^k preparation followed by staining with Coomassie blue showed only one band of relative molecular mass (M_r) $\sim 33,000$ and one band of $M_r \sim 28,000$ with no detectable impurities. NBD-HEL(46-61) was obtained by chemical coupling of 7-fluoro-4-nitrobenzo-2-oxa-1, 3-diazole (NBD-F) to HPLC-purified HEL(46-61) (ref. 26). NBD-HEL(46-61) was identified as amino-terminal-labelled HEL(46-61) with absorption maxima at 340 and 480 nm¹³, and HPLC purified. Various concentrations of NBD-HEL(46-61) were incubated for 5 h with 8.64 nmol I-A^k in 0.25% Triton X-100 at a final volume of 800 μl . Samples were transferred into 6.4-mm diameter Spectra/Por 2 membrane tubing (M_r cutoff, 12,000–14,000) and dialysis was performed at 37 °C against 50 ml of 0.25% Triton X-100 in PBS. Following dialysis to equilibrium, samples were assayed for fluorescence intensity by excitation at 465 nm and emission at 535 nm using an LS-5 Perkin-Elmer fluorimeter. The data were analysed by linear regression. At maximal levels of NBD-HEL(46-61) offered, $\sim 67\%$ of the total I-A^k sites were bound. Linearity of the Scatchard plot is consistent with homogeneity of the I-A^k preparation. Concentration of NBD-HEL(46-61)_{free} was determined by comparison of dialysate fluorescence with a standard curve of NBD-HEL(46-61) in 0.25% Triton X-100. Concentration of NBD-HEL(46-61)_{total} was determined by comparison of sample fluorescence to a standard curve of NBD-HEL(46-61) in 0.25% Triton X-100 containing 10.8 μM purified I-A^k. Concentration of NBD-HEL(46-61)_{bound} was calculated by subtraction of NBD-HEL(46-61)_{free} from NBD-HEL(46-61)_{total}. At all concentrations of NBD-HEL(46-61) used, the recovery of total fluorescence units was $>96\%$. The values on the x and y axes in *a* are expressed in nmol NBD-HEL(46-61). We found no differences in the wavelength of maximum absorption/emission nor in the quantum yield of NBD-HEL(46-61)_{free} compared with NBD-HEL(46-61)_{bound}.

an irrelevant transmembrane protein. In our particular assay system the NBD-HEL(46-61) and an Ia molecule must associate with a K_d of $\leq 50 \mu\text{M}$ before we can detect it. NBD-HEL(46-61) could actually be binding to the I-A^d molecule, but with a K_d below the level of detection in our system. Although our binding data indicate a stable association of I-A^k and peptide in Triton, it is possible that this association is strengthened on contact with the T-cell receptor. Of course, it is also possible that a peptide-Ia complex could further interact with other presenting cell membrane components before functional complexes can be formed. Recently, Watts *et al.* have shown that planar membranes containing incorporated I-A^d are able to present a peptide digest of ovalbumin to ovalbumin-specific, I-A^d-restricted T-cell hybridomas¹⁶. Indeed, our preparation of I-A^k incorporated into planar membranes in the presence of HEL(46-61) stimulates our T-cell hybridomas (B.P.B., P.M.A. and E.R.U., in preparation). These results argue that Ia and processed antigen in the presence of membrane phospholipids are at least a

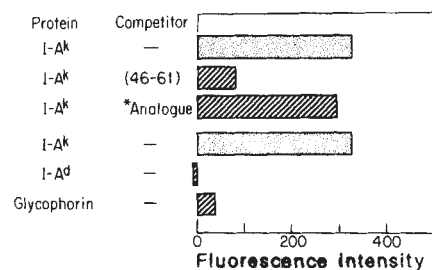


Fig. 3 Binding of NBD-(46-61) to the I-A^k molecule is inhibited by native HEL(46-61) and is haplotype-specific. Binding was measured by equilibrium dialysis as described in Fig. 2 legend, except that a 10-fold molar excess of either native HEL(46-61) or a synthetic HEL(46-61) analogue (Asn-Thr-Asp-Gly-Ser-Thr-Asp-Tyr-Ser-Val-Phe-Thr-Tyr-Ala-Gly-Lys) was mixed with NBD-HEL(46-61) before incubation with I-A^k. Binding of NBD-HEL(46-61) to either I-A^d or glycophorin was measured using 86.4 or 43.2 nmol protein, respectively. The x-axis shows the fluorescence intensity of bound NBD-HEL(46-61) obtained by subtraction of NBD-HEL(46-61)_{free} from the total fluorescence. NBD-HEL(46-61), HEL(46-61) and the HEL(46-61) analogue were all purified by reverse-phase HPLC.

minimally sufficient system with which to present antigen to T hybridomas.

Note that several laboratories had attempted to measure specific binding of various radiolabelled antigens (native, processed or synthetic) to intact Ia-bearing cells without much success^{17–19}. Most attempts using fresh cells resulted in a high background of nonspecific binding. In our system, which contained relatively high concentrations of I-A^k (10.8 μM) and NBD-HEL(46-61) (35 μM), a maximum of 5–6% of peptide bound specifically to I-A^k. To detect the interaction of NBD-HEL(46-61) with an equivalent number of I-A^k sites on intact cells would require a large number of TA3 cells; however, it is impossible to achieve the same concentration of I-A^k sites with intact cells compared with purified I-A^k.

Because many different peptides are presented in the context of a given haplotype, it follows that we would expect competition for the binding to a given I-A molecule by both foreign and native peptides and/or multiple binding sites on the Ia molecule. We agree that macrophages and antigen-presenting cells do not discriminate between self and non-self², and we have shown that peptides of autologous lysozyme compete both in antigen presentation and for binding to I-A^k (P.M.A., B.P.B. and E.R.U., in preparation). Recent experiments are also compatible with competition of more than one peptide antigen for binding to Ia molecules^{20,21}. Finally, there are observations suggesting that multiple functional sites exist on a single Ia molecule which may allow it to interact in a specific manner with various peptide antigens^{22–24}. Of course, increasing the number of possible functional Ia restriction sites, either by combinatorial association of α - and β -chains or by using more than one site per molecule, should increase the number of ways Ia molecules can interact with antigen and function in antigen presentation. Furthermore, the binding of a single peptide to a single Ia molecule can generate several different antigenic determinants⁹.

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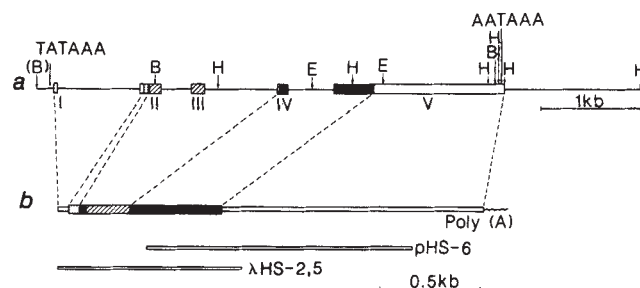


Fig. 1 *a*, Structure of human pulmonary surfactant apoprotein (PSAP) gene. Restriction enzyme cleavage sites located in the 6.0-kilobase (kb) segment of cloned human genomic DNA are indicated (E, *EcoRI*; B, *BamHI*; H, *HindIII*). Exons are represented by boxes, with the putative signal peptide denoted by stippling, the collagen-like segment shown as the cross-hatched region, and the non-collagen sequences corresponding to the filled-in portions. *b*, Schematic diagram of human PSAP mRNA, showing regions present in each exon of the gene. Translated sequences are depicted by the wide box, with the different coding regions of the protein denoted as above. The extent and overlap of cDNA clones are shown by the thick bars below the diagram.

Methods. **Gene cloning:** A library of human genomic DNA cloned in bacteriophage Charon 28 (ref. 33) was screened on nitrocellulose filters⁴⁸ with ³²P-labelled canine PSAP cDNA pDS-1 (ref. 8). Duplicate filters carrying DNA from a total of 1.5×10^6 phage plaques were hybridized with 5×10^5 c.p.m. ³²P-labelled pDS-1 probe in 40% formamide, $5 \times \text{SSC}$ ($1 \times \text{SSC}$ is 0.15 M NaCl, 0.015 M sodium citrate, pH 7.5), 0.05% SDS, $5 \times \text{Denhardt's}$ (0.02% bovine serum albumin, 0.02% Ficoll, 0.02% polyvinyl pyrrolidone), $50 \mu\text{g ml}^{-1}$ yeast transfer and $50 \mu\text{g ml}^{-1}$ denatured, sheared salmon-sperm DNA at 37°C for 16 h. Following hybridization, the filters were washed twice at 50°C for 30 min in $2 \times \text{SSC}$, 0.1% SDS, dried and autoradiographed on Kodak XAR film with Dupont Cronex intensifying screens until complete exposures were obtained. One strongly hybridizing phage containing 14 kb of human genomic DNA was isolated. The positive clone was digested with *BamHI* and DNA fragments of 3.5, 1.2 (the 5' *BamHI* site directly adjacent to the arm of the phage vector was presumably artificially generated through the library construction) and 4.7 kb were purified and subcloned in pBR322 (pPSAPb3.5, pPSAPb1.2, pPSAPb4.7) by standard techniques³⁴. Restriction enzyme mapping and Southern blot analysis³⁵ of the subcloned genomic fragments using ³²P-labelled pDS-1 probes allowed construction of the gene map. **cDNA cloning:** *a*, Fetal human lung poly(A)⁺ RNA from a 24-week-old fetus was isolated by the guanidinium isothiocyanate technique³⁴ and used to prepare a dT-primed cDNA library cloned in dG-tailed pBR322. Colony filters were screened as described previously⁸ with ³²P-labelled pDS-1 cDNA under the hybridization conditions described above. A single positive clone, pHS-6, was isolated and further characterized by nucleotide sequence analysis. *b*, An adult lung cDNA library was obtained from Dr Barry Greenberg. Starting with poly(A)⁺ RNA isolated from adult human lung, randomly primed cDNA was prepared and cloned in the bacteriophage vector gt10 using *EcoRI* linkers, as described by Huynh and co-workers³⁶. Phage plaques were screened with a ³²P-labelled hybridization probe prepared from pHS-6. Plaque filters were hybridized with 5×10^5 c.p.m. ³²P-labelled pHS-6 probe in 50% formamide, $5 \times \text{SSC}$, 0.05% SDS, $5 \times \text{Denhardt's}$, tRNA and salmon sperm DNA at 42°C for 16 h. Filters were washed twice at 50°C for 30 min each in $0.2 \times \text{SSC}$, 0.1% SDS, dried and autoradiographed. Two of the clones carrying long inserts, HS-2 and HS-5, were chosen for further analysis. The 3'-terminus of each clone corresponds to the natural *EcoRI* site within the PSAP coding region. Both clones extend through the 5'-untranslated area, ending within a few nucleotides of one another. Nucleotide sequence determination: Nucleotide sequence of genomic and cDNA clones were established by the chain termination method³⁷ using restriction fragments subcloned into the phage M13 vectors mp8 and mp9 (ref. 38).

Two independently isolated cDNA clones, HS-2 and HS-5, were characterized further by nucleotide-sequence analysis. Both clones contain the entire PSAP coding sequence and all but a few nucleotides of the 5'-untranslated sequences. Both clones overlap with the original cDNA isolate, allowing us to obtain a continuous and nearly full-length sequence of the PSAP mRNA. A comparison of the cDNA sequences with the complete sequence of the genomic clone (Fig. 2) gave a map of intron and exon structure for the human surfactant apoprotein gene (Figs 1, 2). An initiation site for PSAP transcripts probably occurs within 24-37 nucleotides downstream from a consensus recognition sequence for initiation, TATAAA (ref. 10). The 5'-untranslated region of human PSAP is relatively short (52-67 nucleotides) and is encoded by exon I and part of exon II. The 3'-untranslated region is contained within exon V and is quite long (1,304 nucleotides). Two polyadenylation signal sequences, AATAAA (ref. 11), are seen in the gene sequence occurring

Isolation and characterization of the human pulmonary surfactant apoprotein gene

R. T. J. ler White, Deborah Damm, Judith Miller, Kaye Spratt, James Schilling, Samuel Hawgood*, Brad Benson & Barbara Cordell†

California Biotechnology Inc., 2450 Bayshore Frontage Road, Mountain View, California 94043, USA

* Cardiovascular Research Institute and Department of Pediatrics, University of California, San Francisco, California 94143, USA

Pulmonary surfactant is a phospholipid-protein complex which serves to lower the surface tension at the air-liquid interface in the alveoli of the mammalian lung and is essential for normal respiration¹. Inadequate levels of surfactant at birth, a frequent situation in premature infants, results in respiratory failure. In all species examined, surfactant is composed primarily of dipalmitoylphosphatidylcholine and two major protein species of relative molecular mass (M_r) 32,000 (32K) and 10K (refs 2-5). Reconstitution *in vitro* of purified 32K pulmonary surfactant apoprotein (PSAP) with synthetic lipids forms a lipoprotein complex that lowers surface tension by spreading to create a thin interfacial film^{6,7}. Here we describe the cloning of the human PSAP gene and complementary DNA, and discuss features of the unusual encoded protein.

Recently we isolated a full-length cDNA encoding the canine 32K PSAP⁸; we used this cDNA in reduced stringency hybridization conditions to screen a human genomic library constructed in bacteriophage Charon 28 (Fig. 1 legend). One hybridizing clone was chosen as the most likely candidate for encoding human PSAP, as it hybridized more intensely with the canine cDNA. Partial sequence analysis of this genomic isolate revealed extensive coding homology (77%) with the canine clone. Whereas the homology to canine PSAP enabled us to assign coding exons tentatively within the human gene sequence, to delineate the human coding regions with certainty we isolated and characterized human PSAP cDNA clones.

A cDNA library was first prepared from poly(A)⁺ RNA derived from fetal lung tissue and screened with canine PSAP cDNA. A single positive clone, pHS-6, was isolated from ~125,000 recombinants. By nucleotide sequence analysis, pHS-6 was shown to encode the carboxy-terminal half of PSAP and to contain a long 3'-untranslated region of the messenger RNA. Using pHS-6 as a probe to rescreen the fetal library, no additional PSAP-specific clones were obtained. Because pulmonary surfactant is synthesized late in fetal maturation⁹, we therefore obtained a cDNA library prepared with poly(A)⁺ RNA isolated from adult human lung. The partial human PSAP cDNA, pHS-6, was again used to screen the adult library and detected many positively hybridizing clones; at least 50-fold more PSAP clones were found derived from adult than from fetal tissue. The apparent increase in PSAP transcripts in the adult human lung suggests that the developmental regulation of this gene occurs at the transcriptional level.

† To whom correspondence should be addressed.

within 15 base pairs of each other near the end of the 3'-untranslated region. We conclude from S_1 analysis¹² using total adult lung poly(A)⁺ RNA (data not shown) that only the proximal polyadenylation signal is used in the maturation of PSAP transcripts.

Roughly 100 base pairs upstream from the TATAAA sequence preceding exon I of the human PSAP gene, a potential binding site for the glucocorticoid receptor can be identified. The sequence GAACATGCTGTG shares identity with several receptor binding sequences located near or within many mammalian

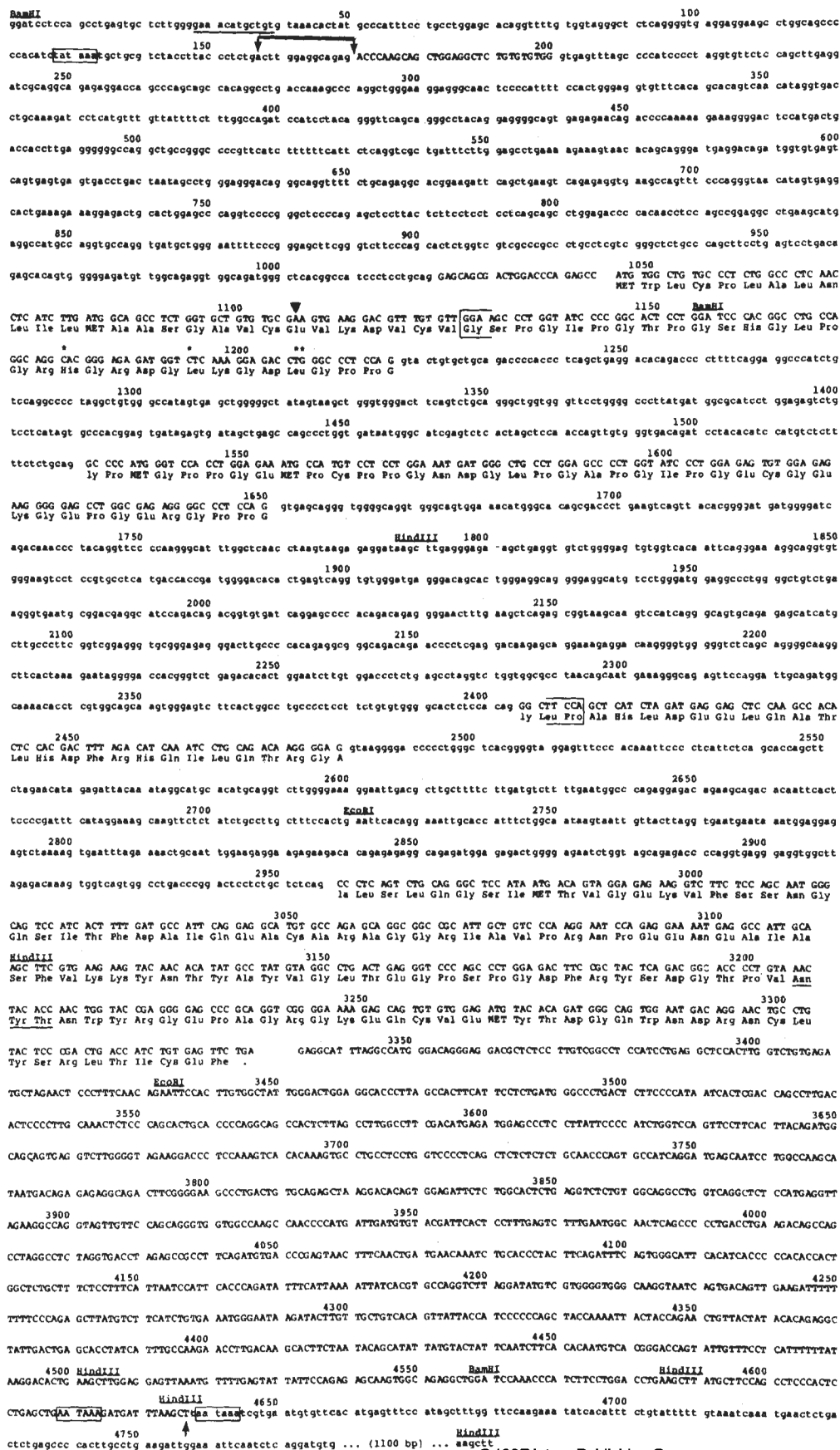


Fig. 2 Nucleotide sequence of human PSAP gene. Nucleotides are numbered from the first *Bam*HI site. Flanking, untranslated and intervening sequences are represented by lower-case letters, and coding sequences by upper-case letters. The derived amino-acid sequence is shown below the appropriate codons. Restriction enzyme recognition sites are indicated above the sequence. The TATAAA box starting at nucleotide 128 and the two polyadenylation signals (AATAAA) at nucleotides 4,619 and 4,639 are boxed. The region containing the presumptive transcription start site is outlined between the vertical arrows. The poly(A) addition site at nucleotide 4,637 is indicated by an arrow. * Indicates single nucleotide differences between the human gene sequence and the human PSAP cDNA sequence. A potential binding site for the glucocorticoid hormone-receptor complex starting at nucleotide 28 is underlined as is the glycosylation site at amino-acid residue 198. The amino-terminal amino acid (Glu) at residue 21 seen in human alveolar proteinosis protein is indicated by a solid triangle and the collagen-like region is bracketed.

Methods. Subcloned *Bam*HI fragments of the human PSAP gene (Fig. 1) were mapped by restriction enzyme analysis, and appropriate DNA fragments were purified and subcloned into phage M13 vectors mp8 and mp9 for dideoxy sequencing. The entire sequence of the inserts was determined in both orientations. Splice sites were confirmed by nucleotide sequence analysis of the cDNA clones, HS-2 and HS-5. The position of the polyadenylation site was determined by S_1 nuclease analysis¹² of adult human lung RNA, using a 32 P-labelled DNA probe derived from the cloned human PSAP gene.

genes known to be regulated by glucocorticoids¹³⁻¹⁵. Extensive *in vivo*^{16,17} and *in vitro*¹⁸⁻²⁰ evidence suggests that glucocorticoids regulate surfactant synthesis. Smith and co-workers have recently shown that^{21,22} glucocorticoids indirectly enhance the synthesis of surfactant phospholipids in type II alveolar cells, but the effect of the steroid hormone on the synthesis of the protein moiety of surfactant was not examined. The presence of a potential glucocorticoid receptor binding site in close proximity to the PSAP gene could suggest that this protein is directly regulated by glucocorticoids.

The 248-amino-acid sequence deduced by the single open reading frame of the human PSAP cDNA clones is also encoded by the genomic isolate. The most striking feature of human PSAP is the collagen-like region characterized by reiterations of Gly-X-Y triplets where Y is frequently a proline hydroxylated post-translationally²³. Twenty collagen-like repeating triplets are encoded on three exons (Figs 1, 2). Exon III is composed almost exclusively of Gly-X-Y repeats (12 triplets out of a possible 13) and hence is similar in genetic structure to collagen genes, which are made up of many short exons each usually containing just 6 Gly-X-Y repeats but occasionally containing 12 repeats²³. The distinct structural similarity of PSAP to collagen suggests that these genes, or portions of them, are evolutionary related. PSAP may, therefore, be a member of the collagen-like gene family which includes acetylcholinesterase²⁴ and C1q of complement²⁵, both of which are distinguished by Gly-X-Y repeating triplets. Four nucleotide differences exist between the cDNA and gene sequences. One of these changes is silent. Three other changes alter codon choice; the three alternative codons all occur in the second or third position of Gly-X-Y triplets (Fig. 2). The observed differences presumably reflect individual allelic variation, polymorphic or multiple genes.

The 22-residue amino-acid sequence derived from the N-terminus of a 32K protein isolated from lung lavage of a patient with alveolar proteinosis corresponds exactly with a segment of the protein sequence encoded by the PSAP clones that begins with predicted amino-acid 21 (Fig. 2). This perfect sequence homology indicates that the glycoprotein present in excess in patients with alveolar proteinosis²⁶ is identical to PSAP secreted in normal lungs, and we infer that the N-terminal amino acid of mature human PSAP is the glutamic acid predicted at residue 21. A recent study of peptide maps by Whitsett *et al.*²⁷ demonstrated homology of alveolar proteinosis protein and human PSAP isolated from lung lavage. Similar to canine PSAP⁸, the N-terminus of mature human PSAP is preceded by a highly hydrophobic signal sequence that tags the protein to be processed for secretion²⁸. Lynn has proposed²⁹ that the 32K alveolar proteinosis protein is derived from a larger precursor. Because PSAP and the alveolar proteinosis protein seem to be identical and as the human PSAP gene encodes an unmodified protein of ~28K which has been confirmed by *in vitro* translation of adult lung mRNA (ref. 30 and our unpublished observations), we find it unlikely that the alveolar proteinosis protein is contained within a larger precursor. While there are similarities (molecular size, glycosylation, hydroxylation of prolines) between human PSAP and the protein described by Lynn and co-workers, it is evident from amino-acid sequence comparison that they are not identical.

We have recently demonstrated that, as a result of variable glycosylation³¹, canine PSAP is heterogeneous with respect to relative molecular mass (36-28K). Our own observations indicate a similar heterogeneity in the human protein, which appears as a complex of proteins with the 32K protein being the major species when examined by SDS-polyacrylamide gel electrophoresis. The protein sequence of human PSAP as deduced from the nucleotide sequence contains a site for N-linked glycosylation (Asn 198, Fig. 2) based on the consensus glycosylation site Asn-X-Ser/Thr (ref. 32).

Benson and coworkers⁷ have demonstrated that purified canine PSAP when added to synthetic lipids in the presence of calcium ions generates a mixture with both surface spreading and surface lowering capabilities. We are presently expressing

the human PSAP gene and plan to test the recombinant protein both *in vitro* and *in vivo* for activity.

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Novel developmental specificity in the nervous system of transgenic animals expressing growth hormone fusion genes

L. W. Swanson^{*†}, D. M. Simmons^{*}, J. Arriza^{*‡},
R. Hammer[§], R. Brinster[§], M. G. Rosenfeld^{†||}
& R. M. Evans^{*†}

^{*} Salk Institute for Biological Studies, PO Box 85800, San Diego, California 92138, USA

[†] Howard Hughes Medical Institute Laboratory,

[‡] Department of Biology and ^{||} School of Medicine, University of California, San Diego, La Jolla, California 92093, USA

[§] School of Veterinary Medicine, University of Pennsylvania, Philadelphia, Pennsylvania 19104, USA

The development of methods for introducing foreign genes into the germ line of mice provides an approach for studying mechanisms underlying inducible and developmental gene regulation¹⁻³. Transgenic animals expressing foreign genes have thus been used to test models of the role played by specific DNA sequences in determining cell-specific expression. Results from these experiments suggest that tissue-specific expression is the consequence of a *cis*-acting regulatory sequence⁴⁻¹¹. However, these results do not exclude the possibility that cell-specific expression of some genes might be 'coded' by combinations of regulatory elements. We have previously described the production of transgenic mice from eggs

microinjected with metallothionein-I/growth hormone (MGH) fusion genes¹², and now demonstrate that the juxtaposition of sequences from two different genes can be deciphered by cells to generate novel tissue specificities. Although expression of the endogenous metallothionein and growth hormone genes has not been detected in neuronal cells, transgenic mice clearly express an MGH fusion gene in a restricted subset of neurones. These results suggest a model in which tissue-specific patterns of expression of certain genes are determined by combinations of *cis*-acting regulatory sequences.

For the plasmids used in the present experiments, the structural part of the growth hormone (GH) gene was fused to the promoter region of the mouse metallothionein-I (MT-I) gene (Fig. 1a; refs 12, 13), and it was anticipated that the fusion gene would be expressed in tissues in which endogenous levels of metallothionein are high, for example the liver (Fig. 1b, c). It was, therefore, unexpected to find in transgenic animals exceptionally high levels of the fusion gene expressed in the brain, a tissue normally expressing low levels of MT and no GH (Fig. 1c). These findings led us to examine in more detail the cellular distribution of fusion gene expression, and to determine whether this specificity is a consequence of sequences within the gene or the site of insertion in the genome.

Initial exploration led to the surprising observation that the expression of the fusion gene was highly restricted to several anatomically defined areas of the brain. The most obvious pattern of cell staining was observed in the hypothalamus: immunopositive cells were concentrated in three parts of the hypothalamus including the large neurones in the paraventricular and supraoptic nuclei (Fig. 2a, b). These cells almost certainly synthesize oxytocin or vasopressin, project to the posterior pituitary and are involved in the integration of neuroendocrine and autonomic responses¹⁴. In addition, small cells in the suprachiasmatic nucleus were even more brightly stained, and scattered large neurones were seen throughout many parts of the hypothalamus. In all cases, neuronal staining was blocked by the addition of rat GH (rGH) to both of the anti-GH sera used. No glial or vascular cell types were stained. Identical results were observed with eight animals from five generations of a single transgenic parent (MGH-10 in ref. 12), demonstrating that the MGH fusion gene is consistently expressed in specific subpopulations of neurones in the brains of this pedigree.

The prominent but highly restricted expression of the MGH gene in the hypothalamus led us to examine possible expression in other areas of the brain. Unexpectedly, specific immunostaining was observed in several areas including regions of the neocortex, hippocampus and olfactory cortex in the MGH-10 pedigree. Each animal examined showed a similar pattern of GH immunostaining that was greatly enhanced by colchicine pretreatment, which blocks axonal transport and leads to accumulation of peptides in cell bodies.

Immunoreactive pyramidal cells restricted to layer V of the neocortex (Fig. 2d) were found in all animals expressing the fusion gene in liver and hypothalamus. The cortex is broadly divided into six layers with unique cell types that are morphologically and physiologically distinct. The hypothalamus and neocortex are extensively interconnected with a ring of forebrain structures called the limbic region, which is broadly concerned with the maintenance of homeostasis and includes the complex structure of the hippocampal formation. In the brains of transgenic mice, specific immunostaining was seen in the pyramidal cells of hippocampal field CA3 (Fig. 2c), which is a region dominated by mossy fibre afferents from the adjacent dentate gyrus. Pyramidal cells in the other hippocampal fields (CA1, 2 and 4) were negative, although some interneurons were stained.

Neurones in several other areas of the brain consistently express the fusion gene; these include cells in layer II of the olfactory cortex, the central nucleus of the amygdala, the pars compacta of the substantia nigra and adjacent parts of the ventral tegmental area, and finally, the dorsal motor nucleus of the vagus nerve.

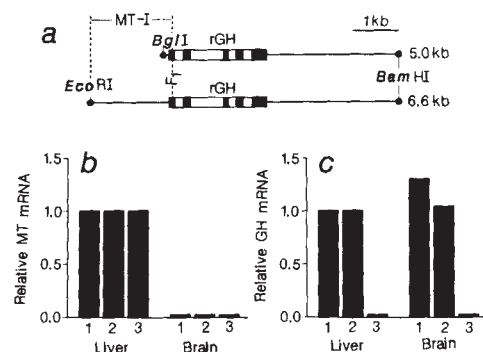


Fig. 1 Structure and expression of metallothionein-growth hormone (MGH) fusion genes. **a**, Restriction fragments from MGH fusion genes that were injected into the male pronucleus of fertilized eggs. Terminal restriction enzyme sites are indicated. The genes are aligned according to the MT-GH fusion boundary. Solid boxes are exons, open boxes are intervening sequences and solid lines are flanking chromosomal sequences. **b**, Relative amount of MT RNA in livers and brains of transgenic (1 and 2) and normal control (3) mice, as detected by slot-blot hybridization with nick-translated MT-I complementary DNA as probe. **c**, Relative levels of GH RNA in livers and brains of transgenic (1 and 2) and normal (3) mice. Rat growth hormone cDNA was used as probe.

Methods. The MGH-10 pedigree was established from a single founder mouse¹² and has been maintained continuously for 3 years. The fusion gene is inherited as a single autosomal dominant allele. Two transgenic mice from the MGH-10 pedigree and one non-transgenic littermate were maintained on 76 mM ZnSO₄ in their drinking water for 1 week to induce maximally heavy metal-dependent MT and MGH gene expression. The animals were killed and total RNA was prepared from the livers and brains. For quantitation, samples were denatured in formaldehyde and 0.5, 5 and 10 µg of RNA from each tissue were slot-blotted onto nitrocellulose. The blot with 0.5 µg of RNA was hybridized with 5 × 10⁵ c.p.m. ml⁻¹ of a nick-translated 18S RNA genomic clone to ensure that we were applying equivalent amounts of RNA from each animal. The blot with 5 µg of RNA per slot was hybridized with a nick-translated DNA fragment containing the MT gene at 2 × 10⁶ c.p.m. ml⁻¹ (ref. 17). The blot with 10 µg of RNA was probed with a nick-translated rat GH cDNA fragment¹⁸ at 2 × 10⁶ c.p.m. ml⁻¹. The blots were hybridized and exposed to X-ray film, and bands were quantitated by scanning densitometry with a Helena optical densitometer. Results are reported as relative levels, arbitrarily assigning the liver of animal 1 at 1.0. In this pedigree the fusion gene was almost exactly twofold more transcriptionally active than the endogenous MT-I gene¹⁸.

In situ hybridization studies were initiated to examine independently the expression of the MGH gene. The regions of most intense immunoreactivity (paraventricular nucleus and supraoptic nucleus) were also the most intensely reactive by hybridization analysis with growth hormone probes. Tissue sections from non-transgenic animals were completely negative. Figure 3 shows both *in situ* analyses and a schematic representation of the remarkably discrete neural expression of the fusion gene.

To determine whether the site of chromosomal integration has a critical role in determining the pattern of MGH expression in neurones, five other integrations of the MT-rGH gene into hybrid mouse strains¹², one into the dwarf (*lit*) mouse¹⁵, and two integrations of the MT-hGH gene¹³, were examined in 11 animals. In each brain, the pattern of GH immunostaining in the hypothalamus was examined in detail, and was identical to that described for the MGH-10 pedigree, although the intensity of staining was variable.

These data suggest strongly that the precise site of integration into the genome does not have a critical role in determining which neurones in the brain express the fusion gene, although it could influence the relative level of gene expression.

If sequences in the MT promoter determine the specific pattern of MGH gene expression in the brain of transgenic mice, expression of the endogenous MT-I gene should have an identical distribution. Antiserum to rat MT-I consistently stained

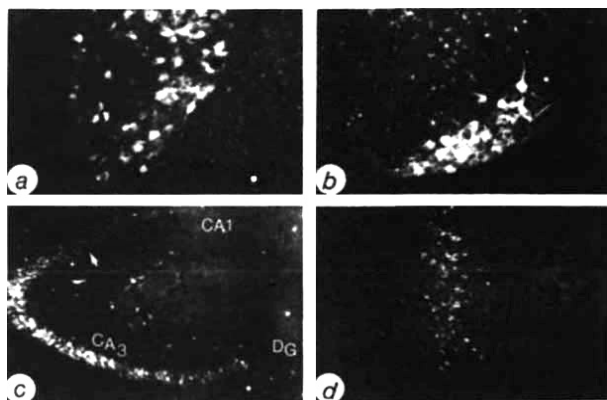


Fig. 2 *a, b*, Frontal sections through the hypothalamus of an MGH-10 animal. Large neurones in the paraventricular (*a*) and supraoptic (*b*) nuclei stained with an antiserum to mouse growth hormone. Small bright patches of staining outside the nuclei were autofluorescent, and cannot be distinguished from specific immunofluorescence in these black-and-white photomicrographs. $\times 75$. *c*, Growth hormone immunostaining in cell bodies in the hippocampus is confined to the pyramidal cell layer in field CA3, and to the region of interneurons in the hilus of the dentate gyrus (DG), and in fields CA1 and CA3. The arrowhead shows the boundary between fields CA1 and CA2; the fimbria is in the lower left-hand corner. $\times 38$. *d*, Stained pyramidal cell bodies in layer V of the junctional region between the somatic sensory (upper half) and motor (lower half) cortex on the left side of the brain. The corpus collosum is to the far left and the pial surface is to the right. $\times 38$.

Methods. Animals were deeply anaesthetized with an intra-peritoneal injection of chloral hydrate, and perfused through the heart according to a modified pH change method that uses mixtures of paraformaldehyde and glutaraldehyde at 4 °C¹⁹. This method was specifically designed for cytoplasmic proteins such as metallothionein, and for peptides²⁰. The brains and livers were postfixed overnight in 4% paraformaldehyde/0.1% glutaraldehyde (pH 9.5) with 15% sucrose. The tissue was frozen with dry ice and 20- μ m-thick sections were cut on a sliding microtome and collected in ice-cold potassium phosphate-buffered saline (KPBS). Free-floating sections were then processed for indirect immunofluorescence, using conventional methods described in detail elsewhere¹⁹. Stained sections were mounted on glass slides, coverslipped with glycerol (pH 8.6), and viewed with a Leitz Dialux 20 fluorescence microscope equipped with Ploem illumination and a 100 W Hg light source. Five antisera to growth hormone were used. Three antisera raised in monkey against rGH were provided by Dr A. F. Parlow (Harbor-UCLA Medical Center, Torrance, California): one (NIH₁) was used at a dilution of 1:400, another (NIH₂) was used at a dilution of 1:4,000, and a third (LA) at a dilution of 1:4,000. The fourth antiserum was raised in a monkey against mouse GH, and was provided by Dr W. P. Vanderlaan (Whittier Institute, La Jolla, California); it was used at a dilution of 1:400 and showed the same staining pattern as the anti-rGH sera. The fifth antiserum, also given by Dr W. P. Vanderlaan, was raised in a rabbit against human GH, and was used at a dilution of 1:10,000. Three of these antisera showed no immunostaining in the brain or liver of control mice and rats, and staining in transgenic mice was completely blocked by the addition of 100 pg of GH to a 1:400 dilution of the antiserum. All the transgenic mice with a rGH fusion gene were stained with the anti-mouse GH serum, and the staining pattern in the brains described in the text was not affected by the addition of 100 pg of synthetic vasopressin or oxytocin (Sigma) to a 1:400 dilution of the antiserum. All antisera to mouse or rat GH gave the same staining pattern as judged on adjacent sections. An antiserum raised in a rabbit to rat liver metallothionein-I was supplied by Dr P. C. Huang (Johns Hopkins University), and was used at a dilution of 1:2,500. Staining in the liver and brain was considerably reduced by the addition of 20 μ g of MT-I to a 1:2,500 dilution of the antiserum²¹. Secondary antisera raised in goats included an affinity-purified, anti-rabbit IgG conjugated with fluorescein, purchased from Tago (Burlingame, Louisiana) (1:200 dilution); an anti-monkey IgG conjugated with fluorescein, from Cappel (Malvern, Pennsylvania) (1:200 dilution); and affinity-purified anti-mouse IgG conjugated with either fluorescein or rhodamine, purchased from American Qualex (La Mirada, California) (1:100 dilution).

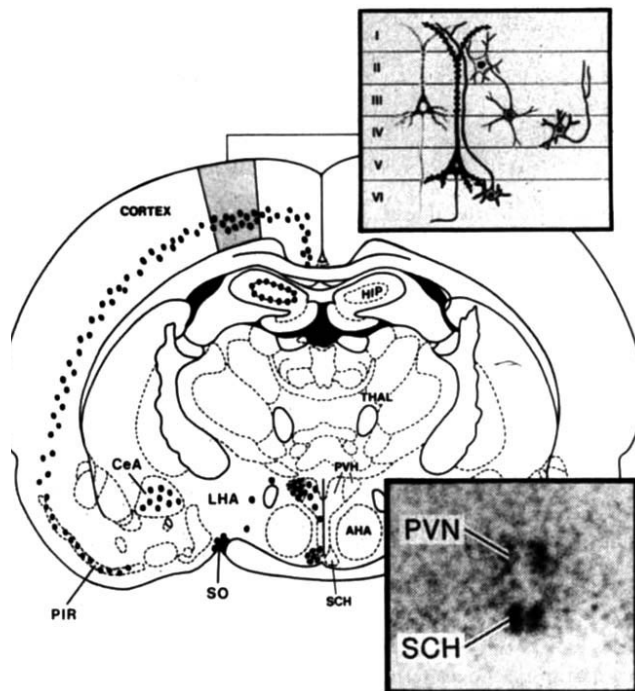


Fig. 3 Summary of the discrete neuronal localization (dots) of GH immunostaining and *in situ* hybridization in a frontal section through the forebrain of a rodent. The upper inset shows that while the cerebral cortex contains many cell types that are distributed through six layers, unequivocal GH staining is confined to large pyramidal cells (black region) in layer V. The lower inset shows the discrete hybridization of a single-stranded GH probe to a coronal section of the hypothalamus of a transgenic mouse. Abbreviations: AHA, anterior hypothalamic area; CeA, central nucleus of the amygdala; HIP, hippocampus; LHA, lateral hypothalamic area; PIR, piriform cortex; PVN, paraventricular nucleus; SCH, supraoptic nucleus; SO, supraoptic nucleus; THAL, thalamus.

Methods. Tissue was fixed as described in Fig. 2 legend. Sections (20 μ m) were mounted on chrome alum-subbed slides¹⁹, air-dried, digested for 30 min at 37 °C with 1 μ g ml⁻¹ proteinase K, acetylated for 10 min at room temperature with 0.25% acetic anhydride in 0.1 M triethanolamine pH 8.0, and dehydrated with ethanol. Slides were hybridized with a single-stranded RNA probe prepared from a SP6 vector containing a GH cDNA insert. Sections were exposed to 10⁶ c.p.m. ml⁻¹ at 48 °C for 16 h^{22,23}; washes included treatment with 20 μ g ml⁻¹ RNase A at 37 °C for 30 min and incubation in 0.1 $\times$ SSC at 48 °C for 30 min. Dehydrated slides were exposed to (Kodak) XAR film at 4 °C for 14 days before developing.

small cells with the appearance of astrocytes in all parts of the white and grey matter, both in normal and transgenic animals; this tentative identification was confirmed in double immunostaining experiments with a monoclonal antibody¹⁶ to the astrocyte marker, S-100, and a polyclonal antiserum (raised in rabbit) to MT-I. Essentially all cells were doubly labelled in this material (Fig. 4), and no evidence for MT staining of neurones was obtained. These results indicate that although the fusion gene and MT-I appear to be co-expressed in hepatocytes, their expression is independently regulated in the brain.

Because the neurones that express the MGH gene are not thought to share a common developmental precursor, do not appear to use a common neurotransmitter, and do not manifest functional or cytological similarities, there is at present no obvious explanation for the fact that the fusion gene is coordinately expressed in these particular neurones. It should be noted, however, that many neuropeptides are also expressed in multiple regions of the central nervous system with no obvious explanation for the origin of the wide variety of patterns observed.

Our results show that the integration sites of the fusion genes do not seem to control the neuronal specificity, because the pattern of fusion gene expression was identical in the brains of



Fig. 4 Co-localization of metallothionein (MT) and the astrocyte-specific marker protein S-100 in the same section through the corpus callosum (a fibre tract) of an MGH-10 animal. The section was incubated in a mixture of a rabbit antiserum to MT and a mouse monoclonal antibody to S-100. MT and S-100 were revealed with a fluorescein-conjugated secondary antiserum and a rhodamine-conjugated secondary antiserum, respectively. The control (CON) panel shows the corpus callosum after incubation in anti-MT serum that was blocked by the addition of MT. $\times 216$.

unrelated transgenic animals. We have further examined the role of the MT-I promoter in directing independently the neuronal specificity by fusing it to other genes. We have recently described the generation of transgenic mice harbouring MT-I linked to the structural gene encoding human growth hormone releasing factor²⁴, although this fusion gene is efficiently expressed in visceral tissues, no evidence for discrete neuronal expression has been found, suggesting that neuronal expression is not simply a consequence of the intrinsic specificity of the metallothionein promoter.

Because metallothionein expression in the brain fails to co-localize with expression of the fusion gene, it is tempting to propose a model that requires sequences within both the 5' flanking and the 3' structural regions of the fusion gene for the observed cellular specificity. According to this hypothesis, sequences present in downstream regions of the growth hormone gene are capable of promoting expression outside the anterior pituitary.

Whatever structural elements are finally identified, the results presented here suggest a model in which developmental expression of some genes may be coded by specific combinations of regulatory sequences. Thus, alterations of unique combinations could alter the patterns of gene expression. Similarly, association of the regulatory sequences from multiple genes could generate novel specificities such as those observed here with the MGH fusion gene. One advantage of such combinatorial regulation would be that it would allow for adaptation, acquisition and expansion of tissue specificity by events that alter the combination of developmental sequences. Such a model would imply that a relatively limited number of such sequences and factors could yield a large and diverse range of tissue specificities.

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Nucleotide sequence evidence for relationship of AIDS retrovirus to lentiviruses

Ing-Ming Chiu*, Abraham Yaniv*, John E. Dahlberg, Arnona Gazit*, Suzanne F. Skuntz*, Steven R. Tronick & Stuart A. Aaronson

Laboratory of Cellular and Molecular Biology, National Cancer Institute, Building 37, Room 1E24, NIH, Bethesda, Maryland 20892, USA

Lentiviruses are a subfamily of retroviruses which have been aetiologically linked to the induction of arthritis, encephalitis, progressive pneumonia and slow neurological diseases in certain species¹. Relatively little is known about their genome structure, mechanisms of pathogenesis or evolutionary relationships with other retroviral subfamilies. In an effort to understand better the mechanisms by which these viruses induce such a variety of chronic diseases, we have molecularly cloned and physically characterized the genomes of caprine arthritis-encephalitis virus (CAEV)² and equine infectious anaemia virus (EIAV) (A.Y. *et al.*, in preparation). The latter, which bears some morphological similarity to the lentiviruses, has yet to be classified definitively as one³. Here, we have determined the nucleotide sequence of a highly conserved region within the CAEV and EIAV *pol* genes. We demonstrate a much closer relationship of their predicted *pol* gene products to that of the presumed aetiological agent of human acquired immune deficiency syndrome (AIDS) than to those of other retroviruses. Additional pairwise comparisons allowed us to generate an evolutionary tree showing that the *pol* genes of lentiviruses and oncoviruses have evolved from a common progenitor.

Previous studies have indicated that the *pol* gene is highly conserved among oncoviral genomes^{4,5}. For example, molecular hybridization studies have revealed that a 5' *pol* gene segment of mouse mammary tumour virus (MMTV), a prototype type B retrovirus, detects corresponding regions of viruses representing each of the major oncoviral genera⁴. Recently, we have shown that this MMTV segment detects homologous sequences within the cloned CAEV genome also². We extended these findings, localizing by reciprocal hybridization the regions within both CAEV and EIAV genomes that shared homology with this MMTV *pol* sequence (data not shown). These homologous regions were used as landmarks for nucleotide sequencing aimed at determining the evolutionary relationships of CAEV and EIAV with other retroviruses.

The 217 amino-acid stretches deduced for the CAEV and EIAV *pol* genes are shown in Fig. 1. The two sequences were compared by using the PRTALN program of Wilbur and Lipman⁶. These sequences were compared with analogous regions of MMTV (K. Dean, personal communication), as well as prototype mammalian type C (Moloney murine leukaemia virus,

* Present addresses: Meloy Laboratories Inc., Revlon Health Care, 6715 Electronic Drive, Springfield, Virginia 22151, USA (I.-M.C.); Department of Human Microbiology, Sackler School of Medicine, Tel Aviv University, Tel Aviv 69978, Israel (A.Y., A.G.).

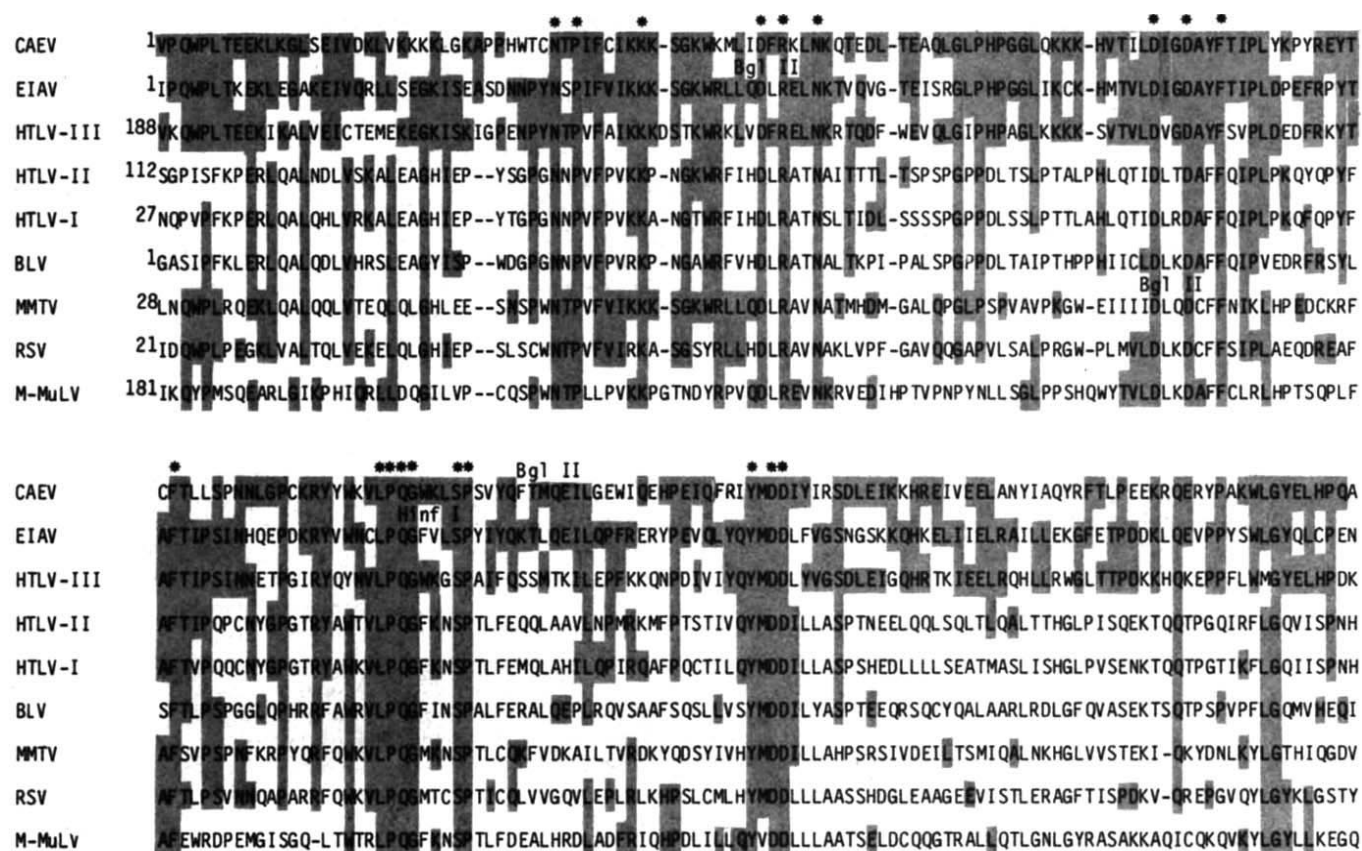


Fig. 1 The alignment of predicted amino-acid sequences encoded by the *pol* genes of CAEV, EIAV, HTLV-III, HTLV-II, HTLV-I, BLV, MMTV, RSV and M-MuLV. The sequences were aligned by the PRTALN program of Wilbur and Lipman⁶. The gaps were introduced to achieve maximum alignment. Amino acids identical to those of either CAEV or EIAV are shaded. The nucleotide sequences of CAEV and EIAV, from which the amino acids are derived, have been deposited in the NIH Nucleic Acid Sequence Data Bank and are available through GENBANK. There is a stretch of 65 nucleotides in MMTV that shows 80% and 70% sequence identity with EIAV and CAEV, respectively, within the homologous regions. This is the most likely explanation for the hybridization observed. The numbering shown at the beginning of each amino-acid sequence corresponds to that given by the original authors. The symbols for the amino acids are: A, alanine; R, arginine; N, asparagine; D, aspartic acid; C, cysteine; E, glutamic acid; Q, glutamine; G, glycine; H, histidine; I, isoleucine; L, leucine; K, lysine; M, methionine; F, phenylalanine; P, proline; S, serine; T, threonine; W, tryptophan; Y, tyrosine; and V, valine. Asterisks indicate the presence of the same amino acid in each sequence.

M-MuLV)⁷, and avian type C (Rous sarcoma virus, RSV⁸) oncoviruses. In addition, we compared these sequences with the as yet unclassified bovine leukaemia virus (BLV)^{9,10}, human T-cell leukaemia viruses HTLV-I¹¹ and -II¹², and the presumed aetiological agent of AIDS¹³⁻¹⁶, HTLV-III.

Figure 1 shows an alignment of all of the *pol* gene sequences; it was necessary to introduce gaps to achieve optimum alignment; however, the gaps were located in the same relative positions. The alignment starts relative to the amino-terminal residue of the BLV reverse transcriptase^{9,10}. As the boundaries of the open reading frames for CAEV and EIAV *pol* genes have not been established, we arbitrarily assigned the amino acid corresponding to the N-terminal residue of the BLV reverse

transcriptase as their respective first amino acids (see Fig. 1). The NH₂ termini of the *pol* gene products of HTLV-I¹¹, MMTV (K. Dean, personal communication) and RSV⁸ are within 30 amino acids upstream from that shown in Fig. 1. AIDS retrovirus¹³⁻¹⁶, HTLV-II¹² and M-MuLV⁷ *pol* genes encode >100 additional amino acids upstream from this point. In the case of M-MuLV, this upstream region encodes a protease responsible for cleavage of *gag* gene products¹⁷.

As shown in Fig. 1, the *pol* gene sequences of CAEV, EIAV and HTLV-III were found to be significantly more similar to each other than to any of the other retroviral sequences analysed. Thus, in each pairwise comparison between CAEV, EIAV and HTLV-III, there was over 50% amino-acid sequence identity

Table 1 Sequence similarity at the amino-terminal regions of retroviral reverse transcriptases

	CAEV	EIAV	HTLV-III	HTLV-II	HTLV-I	BLV	MMTV	RSV	M-MuLV
CAEV		51.2	51.8	29.4	30.4	28.0	30.4	32.2	22.3
EIAV			52.8	31.2	30.0	28.2	33.6	33.1	28.6
HTLV-III				29.3	29.2	26.0	31.6	35.8	25.4
HTLV-II					75.9	53.7	39.8	37.0	32.6
HTLV-I						51.8	39.4	38.9	32.6
BLV							35.6	34.2	29.8
MMTV								47.7	30.3
RSV									32.1

The percentage sequence identity value shown for each pair of retroviruses was obtained from the pairwise amino-acid sequence alignments shown in Fig. 1.

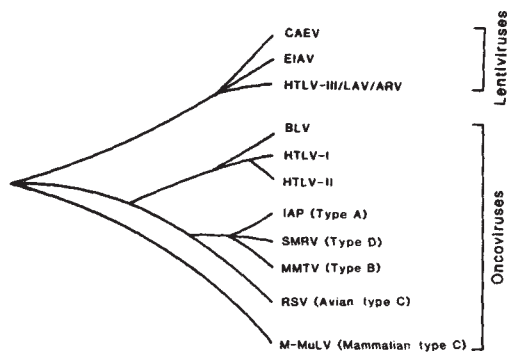


Fig. 2 Evolutionary tree of retroviral *pol* genes. The tree was constructed based on the percentage homology shown in Table 1 for each pair of retroviruses. The distances between the branch-points do not reflect actual divergence times. HTLV-III, LAV (lymphadenopathy-associated virus) and ARV (AIDS-associated retrovirus) are prototype AIDS retroviruses; IAP, intracisternal A-particle.

(Table 1). The homology among different AIDS retrovirus isolates in this region is >99% (refs 13–16). In contrast, we found no more than 36% sequence similarity when the other retroviral *pol* gene sequences were compared with those of either CAEV, EIAV or the AIDS retroviruses (Table 1). The predicted *pol* gene product of HTLV-III, the prototype AIDS retrovirus, was no more related to that of HTLV-II (29.3%), HTLV-I (29.2%) or BLV (26.0%), than to that of RSV (35.8%) or MMTV (31.6%). By comparison, the predicted *pol* gene products of two members of the HTLV family, HTLV-I and HTLV-II, exhibited 75.9% homology. Using the same computer analysis⁶, there were only short stretches of very limited amino-acid sequence homology between HTLV-III and the genomes of oncoviruses in regions outside their *pol* genes.

Table 1 also illustrates other examples of relatively higher *pol* gene homology such as that between BLV and HTLV-I (51.8%) or HTLV-II (53.7%), and that between MMTV and RSV (47.7%). To further substantiate the notion that higher degrees of homology observed between certain retroviral 5' *pol* gene sequences reflected their closer evolutionary relationships, we compared available sequences for the 3' regions of their *pol* genes. Analogous results were derived from such comparisons. HTLV-I and BLV show significantly greater homology (45%) as do MMTV and RSV (39.2%) in their 3' *pol* gene regions⁴. The squirrel monkey retrovirus (SMRV)¹⁸, a prototype mammalian type D virus, also exhibits much closer homology to both MMTV and RSV in its 3' *pol* region⁴. We have shown previously by nucleic acid hybridization that the *pol* gene of the intracisternal A-particle, the prototype type A viral genome, is more closely related to the *pol* genes of MMTV, SMRV and RSV than to those of other oncoviruses¹⁹. Based on all these findings, we were able to construct an evolutionary tree in which retroviral *pol* genes derive from a common progenitor (Fig. 2).

The 3' domain of the RSV *pol* gene encodes endonuclease and DNA binding activities²⁰. The demonstration of highly conserved regions at the 3' *pol* terminus^{4,5} made it possible, through site-directed mutagenesis, to define an important functional domain of the endonuclease that is involved in the specific cleavage of closed circular proviral DNA and integration of the proviral genome^{20–23}. The present study demonstrates a higher degree of relatedness among 5' *pol* gene sequences of retroviruses, uniformly 6–8% greater in pairwise comparisons, than at their 3' regions (Table 1; ref. 4). It will be of interest to investigate the effect of site-specific mutagenesis of this 5' region in efforts to localize even more critical functional domains of this important viral-encoded protein.

There have been contradictory reports concerning the relationship of the AIDS retroviruses to other retroviruses^{24–26}. The nucleic acid hybridization²⁵ and heteroduplex formation

initially observed between HTLV-I and HTLV-III have not been reproduced²⁶, and direct sequence comparisons argue against the validity of the earlier reports^{13–16,24}. Moreover, findings of heteroduplex formation between cloned HTLV-III and visna virus²⁵, an ovine lentivirus, have been challenged by investigators who have failed to detect homology of these viral genomes by filter hybridization techniques²⁶.

Our present findings provide direct evidence at the nucleotide sequence level that the AIDS virus *pol* gene is much more closely related to those of lentiviruses than to those of oncoviruses. As there is evidence that recombination between retroviral genera has played some part in their evolution⁴, it will be of interest to compare the complete sequences of lentiviral genomes with those of other retroviruses to establish more fully their evolutionary relationships. However, there is already immunological evidence indicating a closer relationship among the major structural proteins of lentiviruses and HTLV-III²⁷, and our sequence analysis of the CAEV long terminal repeat (LTR) has revealed a lysine transfer RNA binding site that is similar to those of the AIDS retrovirus and MMTV (L. Sherman *et al.*, in preparation). These results suggest that the greater homology observed by us in the conserved *pol* gene region of HTLV-III and lentiviruses probably extends throughout their genomes.

It is well documented that EIAV and visna viruses can develop novel antigenic variants that can escape temporarily from host immune surveillance^{28,29}. Moreover, genomic analysis of different AIDS retroviruses and lentiviruses such as CAEV has revealed striking heterogeneity in their restriction enzyme maps^{2,13–16}. Our present demonstration that AIDS retroviruses are closely related to the lentivirus subfamily suggests the usefulness of lentiviruses as experimental models for the development of AIDS vaccines. However, our findings also emphasize the challenge that these rapidly evolving retroviruses present in prevention and control of their associated diseases.

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Note added in proof: After submission of this manuscript, the complete sequence of the IAP genome was published³⁰. Comparisons of the IAP amino-acid sequence within the endonuclease region with those of SMRV (50%) and MMTV (49%) substantiate our molecular hybridization data.

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